CENTRAL CORNEAL THICKNESS IN INDIVIDUALS WITH AND WITHOUT PSEUDOEXFOLIATION SYNDROME

Dissertation submitted in

Partial fulfillment of the regulations required for the award of

M.S. DEGREE

In

OPHTHALOMOLOGY

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2014

DECLARATION

I solemnly declare that this dissertation entitled "**CENTRAL CORNEAL THICKNESS IN INDIVIDUALS WITH AND WITHOUT PSEUDO EXFOLIATION SYNDROME"** is a bonafide and genuine research work done by me under the supervision and guidance of **Dr. A. Rajendraprasad MS DO,** Professor and Head of the Department of Ophthalmology, Coimbatore Medical College, Coimbatore.

This is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of regulations required for the M.S. Ophthalmology, Branch III Degree Examination to be held in April 2014.

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This is to certify that the dissertation entitled "**CENTRAL CORNEAL THICKNESS IN INDIVIDUALS WITH AND WITHOUT PSEUDO EXFOLIATION SYNDROME"** is a bonafide research work done by **Dr. S. PRIYADHARSHNI**, Postgraduate in M.S. Ophthalmology, Coimbatore Medical College, Coimbatore under my direct guidance and supervision, to my satisfaction, in partial fulfillment of the regulations required for the award of M.S Degree in Ophthalmology (Branch III).

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ACKNOWLEDGEMENT

I bestowe my sincere thanks to the **DEAN Dr. R. VIMALA, MD,** Coimbatore Medical College Hospital, Coimbatore for permitting me to do this research work.

I am extremely thankful to **Prof.Dr.A.RAJENDRAPRASAD MS DO,** Head of the Department, Ophthalmology, Coimbatore Medical College Hospital for his valuable guidance and moral support which helped me in completing this work successfully.

I am grateful to **Prof. Dr. B. ZAIBUNISSA MS DO,** for her valuable advice and encouragement in the preparation of this dissertation.

I owe my gratitude to my Assistant Professors **Dr. J. Saravanan MS, Dr. C. Jeevakala MS DO, Dr. P. Sumathi MS, Dr. E. Anithaa MS** for helping and guiding me in completing this work.

Thanks to the administrators and nursing staff for having helped me whole heartedly to complete this work.

Finally, I would like to thank all my patients for their immense and patient cooperation.

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INTRODUCTION Glaucoma is one of the leading causes of irreversible blindness throughout the world. WHO statistics indicate that glaucoma is the second leading cause of blindness globally after cataracts. [1]It has been estimated that about 12 milion people are affected by glaucoma in India and the majority of them are undiagnosed. [2] In Southern India, the prevalence of glaucoma has been estimated to be around 2.6% & 90% of these cases have never been diagnosed before, compared to 50% previously undiagnosed in European countries. [1] Glaucoma is defined as a chronic progressive optic neuropathy, caused by various ocular conditions which lead to damage of the optic nerve with loss of visual...

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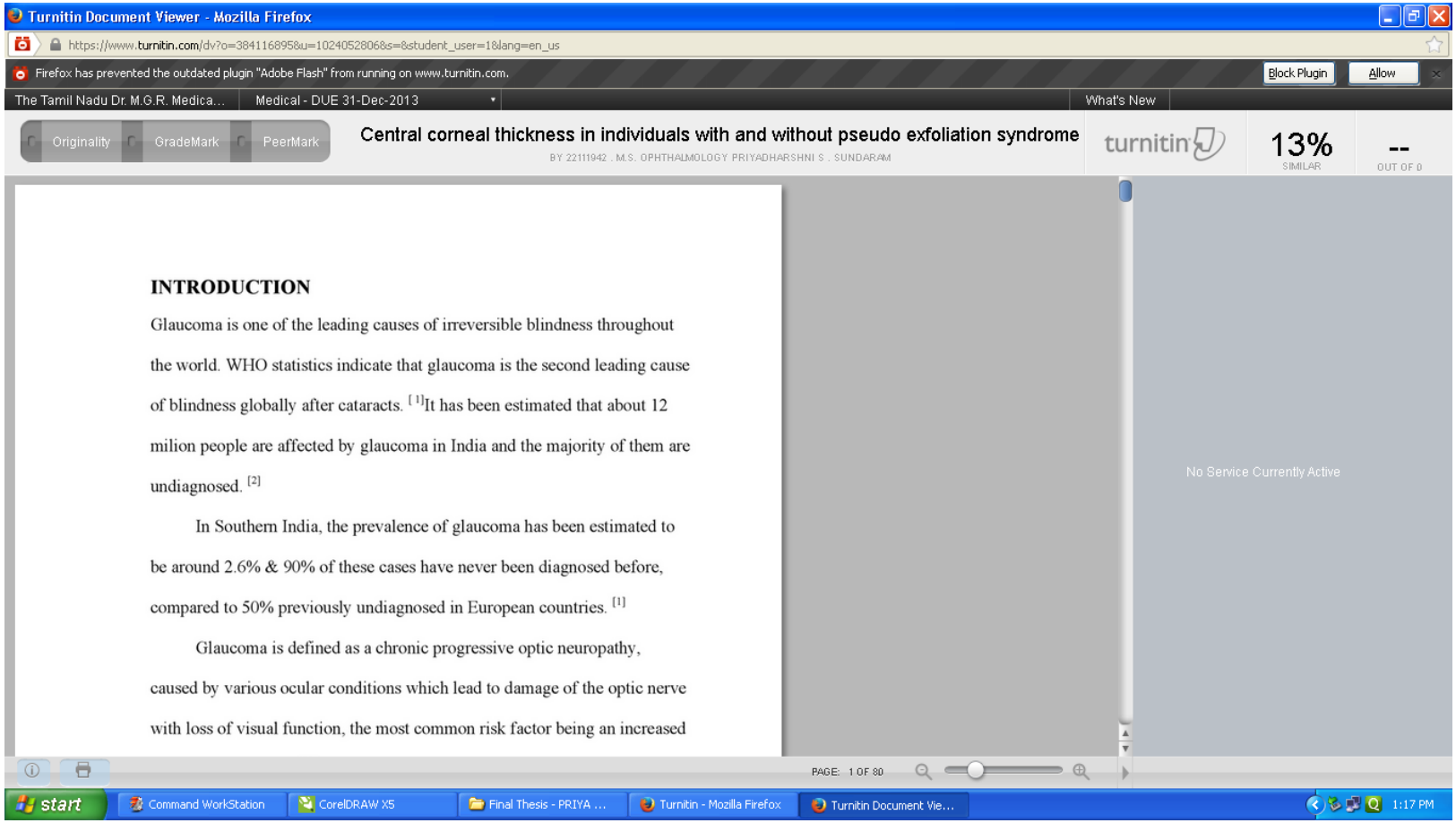
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ABSTRACT

AIM: To compare the central corneal thickness in individuals with and without pseudo exfoliation syndrome.

METHODS: This was a hospital based cross sectional, comparative study. 50 individuals with unilateral or bilateral pseudo exfoliation syndrome (study group) and individuals without pseudo exfoliation syndrome (control group), both without any corneal pathology and glaucoma were included in the study. The CCT was measured by an ultrasonic pachymeter. The IOP was measured by Goldmann applanation tonometer and was adjusted for the CCT values.

RESULTS: There was no significant correlation between CCT, age and gender. The mean CCT was 0.515± 0.07 mm in the control group and 0.501 mm $\pm$ 0.07 mm in study group (P value=0.001). The mean IOP was almost similar in both groups. However, the IOP after CCT adjustment was significantly higher in the study group than the control group.

CONCLUSION: The mean CCT was significantly lower in the individuals with pseudoexfoliation than in individuals without pseudo exfoliation. There was no significant difference in the CCT between the eye with PEXF and its fellow eye in unilateral pseudo exfoliation syndrome.

Key words: Central corneal thickness, pseudo exfoliation syndrome.

ABBREVIATIONS & ACRONYMS

WHO	-	World Health Organization
CCT	-	Central Corneal Thickness
CC	-	Corneal Curvature
PXS	-	Pseudo exfoliation syndrome
PEXF	-	Pseudo exfoliation
BUT	-	Break Up Time
PEXG	-	Pseudo exfoliation glaucoma
POAG	-	Primary Open Angle Glaucoma
PACG	-	Primary Angle Closure Glaucoma
NTG	-	Normal Tension Glaucoma
CACG	-	Chronic Angle Closure Glaucoma
OHT	-	Ocular Hypertension
PIG	-	Pigmentary Glaucoma
IOP	-	Intra Ocular Pressure
OCT	-	Optical Coherence Tomography
GAT	-	Goldmann’s applanation tonometry
C:D ratio	-	Cup:Disc ratio
RBS	-	Random blood sugar
UBM	-	Ultra sound biomicroscopy
OLCR	-	Optical Low Coherence Reflectometry
CMTF	-	Confocal Microscopy - Through Focusing
U/L	-	Unilateral
B/L	-	Bilateral
ANOVA	-	Analysis of Variance

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INTRODUCTION

Glaucoma is one of the leading causes of irreversible blindness throughout the world. WHO statistics indicate that glaucoma is the second leading cause of blindness globally after cataracts. [1] It has been estimated that about 12 million people are affected by glaucoma in India and the majority of them are undiagnosed. [2]

In Southern India, the prevalence of glaucoma has been estimated to be around 2.6% and 90% of these cases have never been diagnosed before, compared to 50% in European countries. [1]

Glaucoma is defined as a chronic progressive optic neuropathy, caused by various ocular conditions which lead to damage of the optic nerve with loss of visual function, the most common risk factor being an increased intra ocular pressure. [3]

Being an important risk factor, the measurement of IOP is an indispensable diagnostic tool in the evaluation of glaucoma. An elevated IOP is the first alarming sign indicative of the patient being affected by or is at risk of developing glaucoma. Rather than a diagnostic tool, IOP measurement plays an important role in the classification of glaucoma and acts as an important guide

to plan the management. An accurate measurement of IOP is required to determine the target pressure to be achieved by treatment, to monitor the response to treatment, to determine the adequacy or a need for change of treatment. Being easily measurable and modifiable, measurement of IOP becomes indispensable in the diagnosis, management and follow up of glaucoma.

Goldmann's applanation tonometry (GAT) is the gold standard technique of measuring the IOP. [4] IOP measurements by GAT are affected by various factors among which Central Corneal Thickness is considered the most important. [5,6] CCT which was initially presumed to be fixed and constant, is now found to be affected by various factors such as race, age, etc.[7,8,9,10] The variations in the CCT significantly influence the IOP measurements by GAT. GAT tends to overestimate the IOP in thicker corneas and underestimates the IOP in thinner corneas. [11, 12]

Apart from the physiological and demographic factors which influence the CCT, certain pathological conditions too significantly affect the CCT. Various studies have shown that CCT varies in different types of glaucoma. The CCT was found to be thicker in patients with ocular hypertension and thinner in cases of normal tension glaucoma, primary open angle glaucoma and pseudo exfoliation glaucoma.[13,14] While thicker corneas lead to over diagnosis of

glaucoma, thinner corneas carry an increased risk of delayed diagnosis due to underestimation of IOP.

Measurement of CCT, therefore, has become an important diagnostic tool in the evaluation of glaucoma. Apart from this, CCT plays an important role in predicting the risk of developing glaucoma in predisposed individuals and determining its progression in established cases. Thinner corneas serve as an independent risk factor for the development of glaucoma compared with thicker corneas. [15] Thus, eyes with thinner corneas are not only predisposed to glaucoma but also carry a risk of underestimation of IOP.

Various studies have shown that CCT is thinner not only in individuals with pseudo exfoliation Glaucoma [16] but also in individuals with Pseudo exfoliation syndrome without glaucoma. [17] Presence of pseudo exfoliation, an established risk factor, when coupled with a thinner CCT confers a greater risk for the development of secondary open angle glaucoma. This, along with a delay in diagnosis due to underestimation of the IOP, worsens the prognosis of pseudo exfoliation glaucoma.

Hence, the measurement of CCT, though mandatory in all cases of glaucoma, special emphasis must be given in those who are at an increased risk of developing glaucoma such as Pseudo exfoliation syndrome to facilitate early

diagnosis, an appropriate management by determining the exact target pressure to be attained and to ensure the adequacy of treatment.

PSEUDOEXFOLIATION SYNDROME

Pseudoexfoliation syndrome was first described by Lindberg in 1917. [18] The prevalence of pseudo exfoliation differs in different population. The prevalence of PEXF in South India is around 6%. [19] The prevalence was found to increase with age and was greater in males. [19, 20] Pseudo exfoliation syndrome rarely occurs below the age of 50 years.

The presence of exfoliative material in autopsy specimens of the heart, lung, liver and kidney in patients with ocular PXS suggested that ocular PXS syndrome is part of a general systemic disorder.[21] PXS is also found to be associated with cardiovascular diseases, cerebral disorders, Alzheimer disease and acute cerebrovascular accidents.[22]

Two single nucleotide polymorphisms in the lysyl oxidase-like 1 (*LOXL1*) gene have been recently identified as strong genetic risk factors for the development of Pseudo exfoliation syndrome and pseudo exfoliation glaucoma. [23, 24]

Pseudo exfoliation occurs due to the progressive accumulation or deposition of abnormal extracellular fibrillo granular material in almost all tissues of the anterior segment of the eye. The production of the exfoliation material is attributed to an increase in the elastic micro fibril components and

imbalance between the matrix metalloproteinases and their inhibitors in the ocular tissues [25, 26, 27] such as the lens epithelium, trabecular meshwork, iris, ciliary processes, conjunctiva and periocular tissue.[28] The exfoliative material gets deposited on the corneal endothelium, trabecular meshwork, iris, pupillary margin, anterior lens capsule, ciliary body and ciliary zonules resulting in various pathologic alterations in the eye. Ultra structural changes have also been documented in the lens capsule, zonules, iris tissue, ciliary body, trabecular meshwork and the conjunctival vessels. [29]

Pseudo exfoliation is diagnosed by the presence of white, flaky, dandruff like, fibrillo granular material on the pupillary margin or the anterior capsule of the lens. A characteristic “three-ring sign” is frequently noted on the anterior lens capsule after pupillary dilatation. It comprises of three zones, a central zone of about 3 mm with visible exfoliation material, a middle clear zone and a peripheral cloudy ring. The central zone is well demarcated with curled edges. The middle clear zone is due to rubbing off of the pseudo exfoliative material by the posterior surface of the iris. This leads to loss of iris pigment resulting in trans-illumination defects.

Pseudo exfoliation in the anterior chamber angle is evident in gonioscopy by the presence of patchy pigment deposition on the trabecular meshwork which is more marked in inferior quadrant and the presence of Sampolesi’s line.

The presence of pseudo exfoliation affects every part of the anterior segment and results in the following complications:

Corneal endothelial decompensation:

Electron microscopic and In Vivo Confocal microscopic studies have demonstrated large clumps of pseudoexfoliation material adherent to the corneal endothelium and a resultant decrease in the endothelial cell density. [30] The endothelial cell loss is attributed to the hypoxic changes in the anterior chamber, accumulation of extracellular matrix and fibroblastic changes in the endothelium. [25, 26, 27] In addition, breakdown of the blood aqueous barrier and the resultant change in aqueous humor affect the cellular metabolism leading to endothelial cell loss. [31, 32]

Decreased Corneal Sensitivity:

The deposition of the exfoliative material and infiltration by dendritic cells within the sub basal nerve plexus results in decreased corneal sensitivity. [30, 31]

Thinning of Central Cornea:

In Vivo Confocal Microscopy demonstrated the presence of pseudo exfoliation material in the anterior stromal layers of the cornea and a reduction

in the stromal cell densities. This was suggested to be the cause of thinner CCT in eyes with PEXF. The thinning was presumed to be due to apoptosis of the keratocytes. [30]

Poor dilatation of the pupil:

PEXF causes atrophy of the dilator papillae resulting in poor pupillary dilatation. [34]

Cataract & Cataract Surgery:

Individuals with PEXF are more prone to develop cataracts and are at higher risk of various complications during cataract surgery. Poor dilatation of the pupil and synechiae between the iris and the peripheral anterior capsule make the surgery difficult. The ciliary zonules are weakened due to PEXF and may result in zonular dehiscence and nucleus drop. The incidence of posterior capsular rent and vitreous loss is also high in eyes with PEXF. [35]

The weakening of ciliary zonules may result in spontaneous subluxation or dislocation of the lens.

Impaired tear film stability:

Significantly lower Schirmer's test and tear film BUT values have been observed in the eyes with PEXF than the eyes without PEXF. The reason for the

same whether due to conjunctival involvement or any other cause is still under research. [36]

Melanin dispersion:

PEXF causes focal disintegration of iris pigment epithelial cells resulting in pigment dispersion. It commonly occurs after pupillary dilatation. [34]

Glaucoma:

20% of eyes with PXS are associated with narrow anterior chamber angles. They are at risk of developing angle closure glaucoma. [37] Subluxation and dislocation of lens may also result in secondary angle closure glaucoma. However, this is relatively rare.

Pseudo exfoliation is the most common cause of secondary open angle glaucoma. The presence of PEXF confers a greater risk of developing glaucoma. The incidence of glaucoma in individuals with PEXF ranges from 9% to 35%. The risk of developing glaucoma is 6 to 10 times higher in the eyes with PXS than those without PXS. [38, 39, 40] The exfoliative material produced by trabecular endothelial cells and other ocular tissues accumulates in the trabecular spaces and causes collapse of the Schlemm's canal resulting in decreased aqueous humor outflow thereby increasing the IOP. [41]

PEXG carries a worse prognosis than POAG because most patients present with advanced optic nerve damage and severe visual field defects. The response to medication is also poor. Retinal vein occlusion has also been associated with pseudoexfoliation glaucoma, which further makes the prognosis more guarded than POAG. [42, 43]

The advanced stage at presentation is attributed to the underestimation of the IOP by GAT because of a thinner CCT. In addition, being an independent risk factor for the development of glaucoma, [15] thinner CCT increases the susceptibility to rapid progression of the disease. The control achieved by treatment is also an apparent one because the IOP is underestimated and the disease keeps progressing with an apparently controlled IOP.

These hazards can be minimized by measuring the CCT in individuals with PXS in order to identify those with thinner corneas who are at increased risk of developing glaucoma and to ensure detailed evaluation and periodic follow up. The IOP must also be adjusted according to the CCT to obtain the true IOP values to facilitate early diagnosis and ensure the adequacy of treatment.

Figure 1.Pseudo exfoliation in pupillary margin

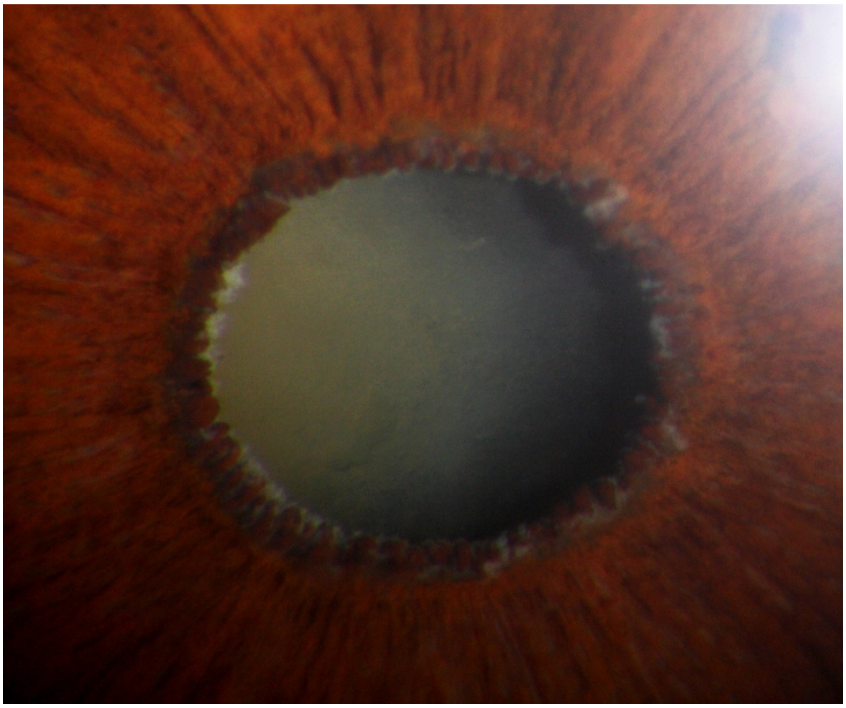


Figure 2. Pseudoexfoliation over anterior lens capsule

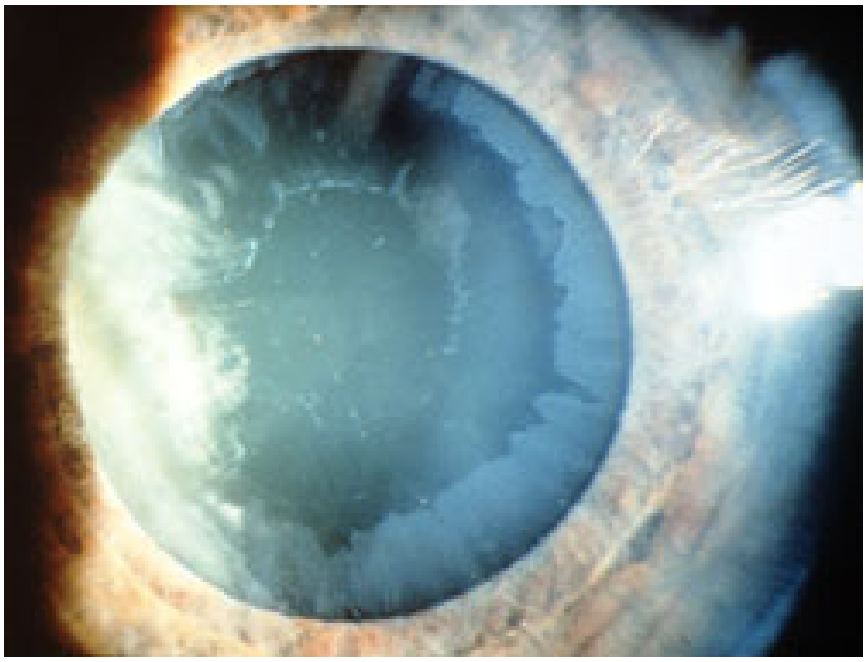
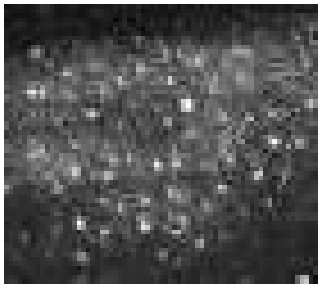


Figure 3. In Vivo Confocal Microscopic view of pseudoexfoliation material

3a. Over the corneal endothelium **3b. Within subbasal Nerve plexus**



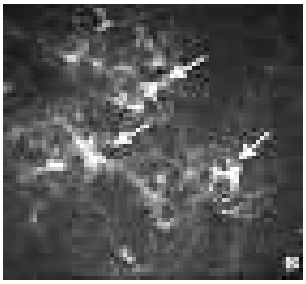
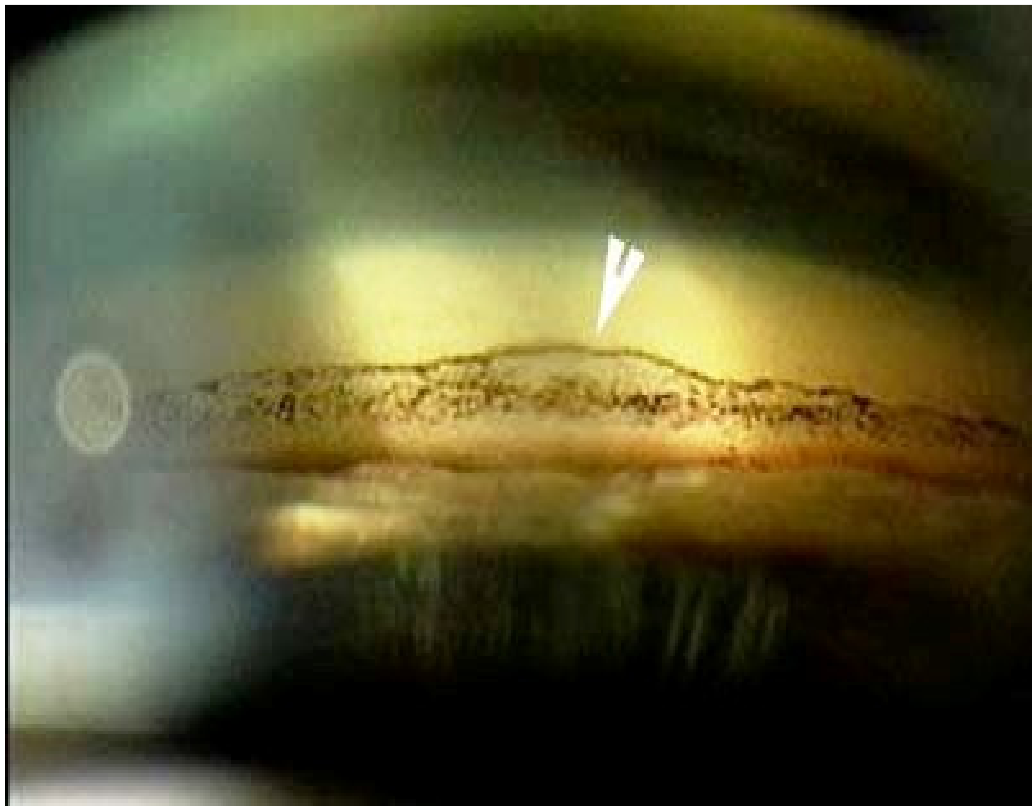


Figure 4. Sampolesi's line on gonioscopy



CENTRAL CORNEAL THICKNESS

Central corneal thickness is one of the very important parameters significantly affecting the IOP measurements by GAT and pulsatile ocular blood flow tonograph. [44]The CCT was initially found to be constant in all individuals. Various studies have found that the CCT is highly variable and is affected by a wide variety of factors:

1. Ethnicity:

CCT shows significant variations in different populations. African-Americans were found to have thinner CCT than Caucasians, Asians and Hispanic population. [7, 45] CCT was found to vary even within the Asian sub-populations. [46]The average CCT in Indian population was found to be 0.520mm. [47] Another study showed that the mean CCT in normal Indian population was about 0.545mm. [48]

2. Age:

CCT is found to decrease with increasing age. However, few studies have shown that no significant correlation exists between age and CCT. [49, 50]

3. Sex:

No definite correlation is found to exist between CCT and sex. Various studies have showed that CCT may be higher, [8] similar [51] or lower [52] in males than females.

4. Corneal curvature:

CCT is found to be thinner in eyes with steeper corneas than flat corneas. [53] Few studies, however, have reported that no significant correlation exists between CCT and corneal curvature. [54]

5. Refractive error:

Myopes are found to be associated with thinner corneas. [55, 56]

6. Ocular surgery:

Orb scan tends to underestimate the CCT measurements after refractive surgery. [57] Intraocular surgeries like cataract extraction are also found to cause thinning of the central cornea. [58]

7. Corneal pathology:

Fuchs's endothelial dystrophy [59] is associated with thicker CCT. The presence of corneal edema tends to underestimate the CCT. [57]

8. Glaucoma:

Ocular hypertensives are found to be associated with thicker CCT while normal tension glaucoma is associated with thinner corneas. POAG, PEXG are also found to have thinner corneas. [13, 14]

9. Pseudoexfoliation:

Eyes with PEXF are associated with thinner CCT than those without PEXF. [17]

10. Systemic diseases:

Diabetes mellitus is associated with increase in CCT. This is attributed to the increased collagen cross linking in the corneal stroma. [60, 61] Chronic Kidney disease, metabolic syndrome and higher body mass index are also found to be associated with thicker CCT. [62]

Few other ocular parameters such as axial length, retinal nerve fiber layer thickness, optic disc size, cup disc ratio have also been found to have significant relationship with CCT. [63, 64]

SIGNIFICANCE OF CCT IN GLAUCOMA:

The role of CCT in IOP measurement by GAT has been well emphasized by various studies. [5, 6] Measurement of CCT followed by adjustment of IOP helps in classifying the patients as ocular hypertension, glaucoma suspects and normal tension glaucomas. [13, 14] Few studies have demonstrated that the CCT measurement has a significant influence on glaucoma management and has led to significant modifications in the treatment options. [65]

CCT itself is found to act as an independent risk factor in predicting the risk of development and the likelihood of progression of glaucoma. [15] The Ocular Hypertension Treatment Study suggested that thinner CCT is a strong predictor of development of glaucoma in eyes with ocular hypertension. [66] Role of CCT as an independent risk factor for development of glaucoma is explained by the fact that sclera is anatomically continuous with the cornea anteriorly and the lamina cribrosa of the optic nerve head posteriorly and therefore changes in the corneal thickness may significantly affect the optic disc too.

The inferior and superior areas of the optic disc are associated with a higher lamina cribrosa pore-to-disc area ratio and a thinner connective tissue support and hence are susceptible to more axonal damage produced by increase

in IOP. Whereas, with a decrease in disc size, the pore-to-disc area ratio also decreases, with a greater connective tissue support. [67, 68, 69] The deformability of a disc with smaller radius is less than that of one with larger radius (Laplace's law). Therefore, for a given IOP, a disc of smaller size experiences less glaucomatous damage than a disc of larger size.

Various studies have shown that CCT has a negative correlation with optic disc area. [15, 70] Thinner CCT is associated with larger disc size and decreased connective tissue support at the lamina cribrosa leading to increased deformability. Such eyes are more prone for glaucomatous damage than eyes with thicker corneas.

MEASUREMENT OF CCT:

Optical pachymetry:

Optical pachymetry measures the distance between the Purkinje Sanson images formed by the anterior and posterior surfaces of the cornea. It employs technique of optical doubling. An image doubling prism mounted on a slit lamp biomicroscope forms two images of the cornea which are viewed through a fixed and rotatable glass plate. The latter is adjusted until the endothelial surface of one image is aligned with the epithelial surface of the other. The corneal thickness is directly measured from a calibrated scale. [71]

Ultrasound pachymetry:

This is a dry contact technique. Sound waves are emitted by a piezoelectric crystal and delivered with a probe. Based on the time required for the sound waves to pass through the cornea and the velocity of sound in the cornea (estimated to be 1630m/sec), the CCT is measured at a frequency of 10 to 20 MHz This is the most common method used, fast and simple to perform. Ultrasound pachymeters are portable, accurate and highly reliable. Corneal thickness as low as 125 microns can be measured. They have an inbuilt algorithm for adjustment of the IOP measured by applanation according to the CCT. They are provided with a printer which enables easy documentation. [57] However, this underestimates CCT in edematous corneas.

Ultrasound Biomicroscopy (UBM):

UBM (50 MHz) and very high frequency ultrasound (70 MHz) require water bath to measure CCT and discern the sublayer details. [57]

Specular microscopy:

Specular microscopy works on optical focusing technique. The reading is set at zero by focusing the interface between the contact element and the epithelial layer. Once the endothelium is focused, the CCT is automatically

displayed. This technique tends to overestimate the CCT compared with other techniques. [57]

Orb scan:

This non-contact method scanning slit based corneal topography incorporates corneal thickness measurement too. [57]

Optical Coherence tomography (OCT):

OCT measures CCT based on optical interferometry. Measurements by OCT are thinner than ultrasound pachymetry. It delineates sub layer details and can measure CCT where ultrasound pachymetry is unable to measure. [57]

Optical Low Coherence Reflectometry (OLCR):

OLCR measures CCT at 18 MHz using infrared radiation. This is incorporated into an excimer laser platform to measure CCT during corneal ablation. [57]

Confocal Microscopy Through Focusing:

CMTF measures CCT by through-focusing a confocal microscope through the thickness of cornea. It also displays the sub layer details and corneal microbiological processes. It cannot be used in eyes with corneal opacities. [57]

Laser Doppler interferometry:

This non-contact technique employs dual beam infra-red laser Doppler interferometry for measuring CCT. [57]

Figure 5. Principle of Optical Pachymetry

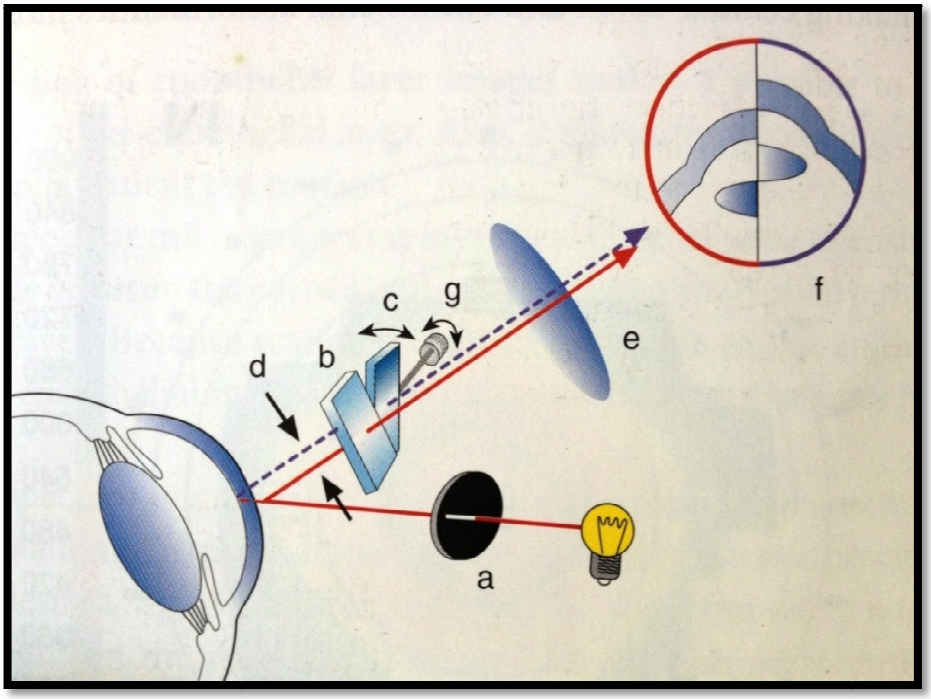


Figure 6. Ultrasound Pachymeter

Figure 7. Calibrations in Ultrasound Pachymeter

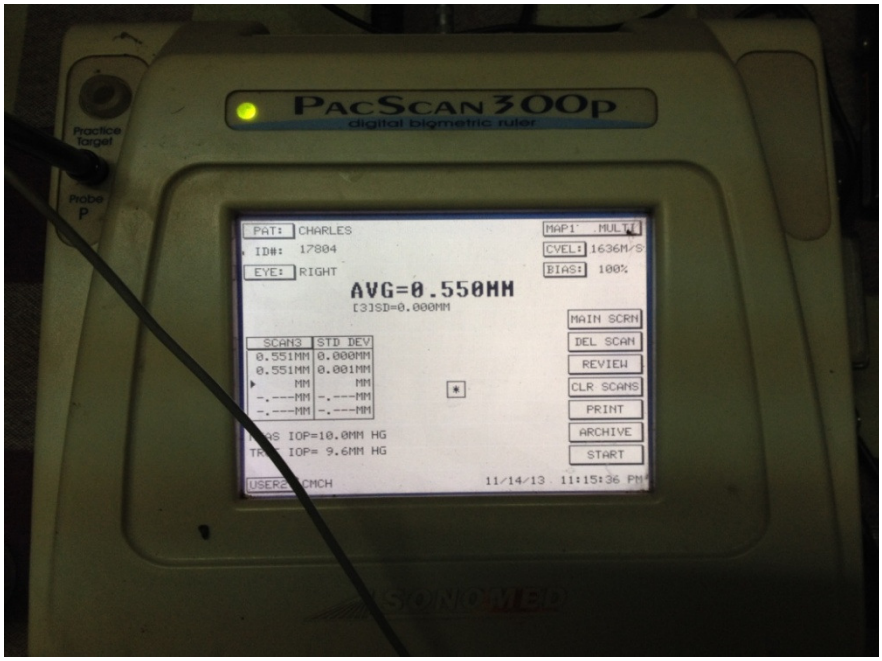


Figure 8. Corneal thickness measurement in UBM

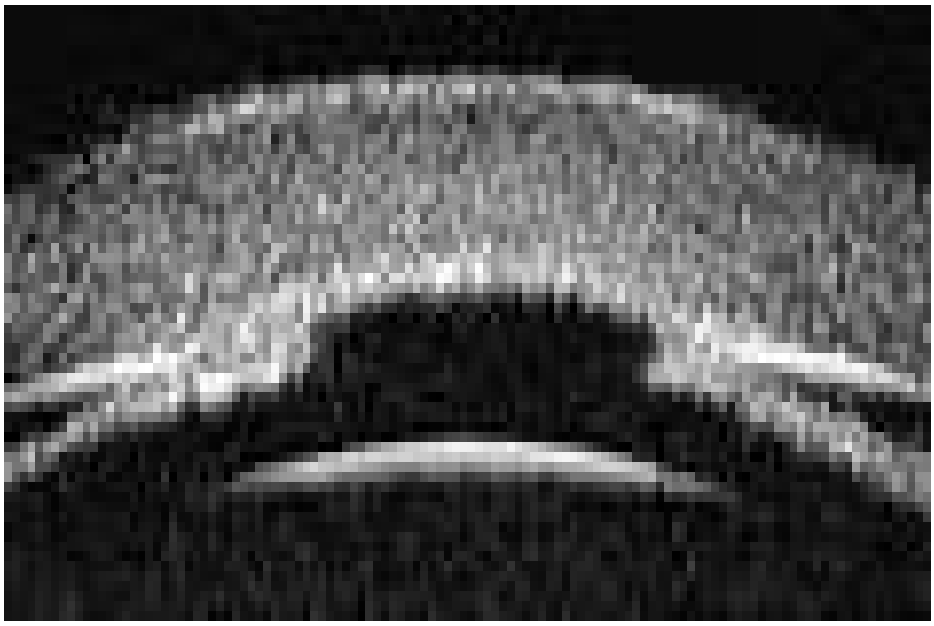


Figure 9. Corneal thickness measurement in anterior segment OCT

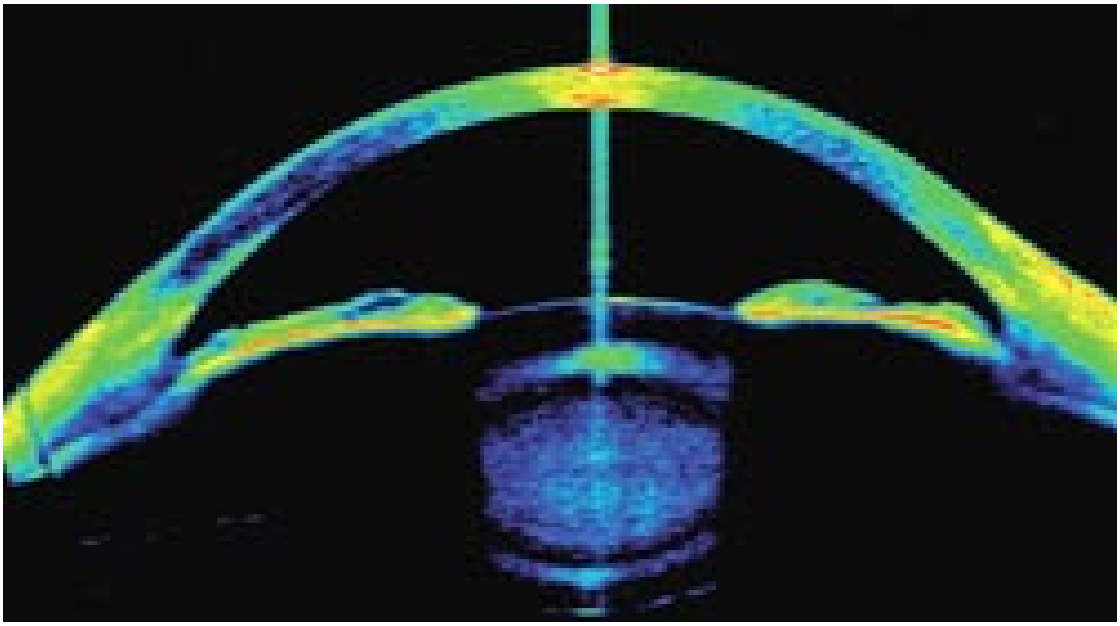


Figure 10. Orbscan

REVIEW OF LITERATURE

Studies by **Wessels et al.** [4] and various others proved that Goldmann applanation tonometry is the most accurate technique for the measurement of IOP.

Goldmann et al. [72] demonstrated the influence of central corneal thickness in the measurement of IOP by GAT. However, they suggested that changes occurring in the CCT significant enough to alter the IOP readings occurred very rarely.

Hansen et al. [73] established that the CCT has a definite correlation with the IOP measurement by GAT. This was also proved by **Ehlers et al.** ,[5] **Whitacre et al.** [6] and various other studies.

Doughty et al. [12] established the fact that GAT overestimates the IOP in thicker corneas and underestimates the IOP in thinner cornea. The same was proven by studies by **Kohlhaas et al**. [11] and various others.

Gordon et al. [66] in 'The Ocular Hypertension Treatment Study' reported the fact that CCT serves as an independent risk factor for the progression of ocular hypertension to primary open angle glaucoma. They found that thinner

CCT was a powerful predictor of the development of glaucoma in ocular hypertension.

Herndon et al. [15] suggested that CCT was a powerful parameter in determining the severity of glaucoma damage at the time of presentation.

Christoph et al [74] reported that a significant negative correlation existed between central corneal thickness and cup disc ratio. A similar correlation was demonstrated by **Memon et al.** [75] They established that thinner corneas had advanced disease at presentation with an increased cup-disc ratio. The same was in accordance with the study by **Tharwat et al.** [76] **Iyamu et al.** [77] suggested that CCT was a better predictor than IOP in identifying individuals at higher risk of developing POAG.

Pakravan et al. [70] reported that eyes with thinner corneas were associated with larger and more deformable optic discs increasing their susceptibility to glaucomatous damage by increased IOP.

CCT, apart from being an important parameter in the estimation of IOP, serves as a powerful factor in predicting the development and progression of glaucoma. A number of studies have been done to assess the thickness of cornea in various types of glaucoma such as primary open angle glaucoma, primary angle closure glaucoma, normal tension glaucoma, pseudo exfoliation

glaucoma, ocular hypertension and conditions like Pseudo exfoliation syndrome where there is an increased risk of glaucoma. Few of such studies are discussed below.

Kenji Inoue et al examined the morphology of corneal endothelium and the central corneal thickness in the eyes of patients with Pseudoexfoliation syndrome (PXS).The central corneal thickness was measured in 26 eyes with PXS (7 eyes o glaucoma patients and 19 eyes of patients without glaucoma) in 21 patients and in 30 patients without PXS, who served as the control group. The corneal endothelial morphology and central corneal thickness (CCT) were compared between the two groups. It was found that the central cornea was significantly thinner in the eyes with PXS (0.529 $\pm$ 0.31 mm) than in the eyes without PXS (0. 547 $\pm$ 0.28 mm) (P= .03). However, it was found that there was no significant difference in the CCT between the eyes with and without glaucoma in tne PXS group. [78]

Mohammad Ali Zare et al. in their presentation "Central Corneal Thickness, Corneal Endothelial Cell Density, and Lens Capsule Thickness in Normotensive Patients with and without Pseudoexfoliation Syndrome" concluded that the mean central corneal thickness in the Pseudoexfoliation syndrome group was significantly lower than control group, but no difference

was found in corneal endothelial density and anterior lens capsule thickness between PXS group and the control group. [17]

Ibrahim F Hepsen et al. studied the corneal curvature & the CCT in eyes with PXS (with & without glaucoma) and compared the values with normal eyes. It was concluded by them that the CC was significantly steeper in the eyes with PXS than the normal subjects. It was also inferred that there was no significant difference in the CCT between the eyes with PXS & the control group. However, a significant difference was observed in the CCT between the subjects with PXS with glaucoma and without glaucoma. The eyes with PXS without glaucoma had a significantly thinner CCT when compared with those eyes with PXS with glaucoma. [79]

Ozcura F et al. retrospectively analyzed the CCT and corneal curvature in 48 eyes with PXS with and without glaucoma (19 with glaucoma, 29 without glaucoma) and compared them with 48 age-matched and sex-matched controls. It was observed that the average CCT was significantly thinner in all PXS eyes without glaucoma than in control eyes. However, there was no difference in the CCT between eyes with PXS and glaucoma and control eyes. No significant difference was found in the keratometry and axial length between the study and control groups. [80]

Spiridon Gorezis et al. measured the central corneal thickness in 60 eyes with primary open-angle glaucoma, 50 eyes with pseudoexfoliation glaucoma, 50 eyes with ocular hypertension using specular microscope and compared the values with the CCT of 60 control eyes without glaucoma or ocular hypertension. They found out that the central corneal thickness was significantly thinner in cases with pseudoexfoliation glaucoma and significantly thicker in cases with ocular hypertension when compared with the control group. [81]

Alpeza-Dunato Z et al. studied the CCT in 34 cases of pseudoexfoliation glaucoma, 31 cases of open angle glaucoma, 28 cases of angle closure glaucoma and 36 normal subjects without glaucoma with a non-contact specular microscope and found that the patients with pseudoexfoliation glaucoma and open angle glaucoma had significantly thinner CCT compared with normal subjects in control group. [16]

Rana Sorkhabi et al on a study about exfoliation syndrome "Retinal Nerve Fiber Layer and Central Corneal Thickness in Patients with Exfoliation Syndrome"; found that retinal nerve fiber layer in exfoliation syndrome group was significantly thinner than control group, but no significant difference was observed in the central corneal thickness between the two groups. [82]

Puska et al. measured the CCT and IOP and assessed the corneal endothelium in 40 normotensive individuals with unilateral PXS and compared the values of the eyes with PXS with their fellow eyes without PXS and observed that the eyes with PXS showed no difference in the corneal endothelial morphology and density. However, the CCT was found to be significantly thicker in the eyes with PXS than the fellow eyes. The IOP was also significantly higher in the eyes with PXS than the fellow eyes after adjustment for CCT. [83]

S Popovic-Suic et al. measured the CCT in 24 cases of Pseudo exfoliation glaucoma, 20 cases of primary open angle glaucoma and 16 normal subjects without glaucoma using an ultrasonic pachymeter. One eye per individual was studied at a time. The mean CCT was almost similar in all the three groups and no statistically significant difference was made between them. They concluded that the CCT was not thinner in PEXG when compared with the other two groups and that thinner CCT was not found to be a risk factor for PEXG. [84]

Sobottka Ventura et al. measured the CCT with an optical low coherence reflectometer in 34 subjects with normal tension glaucoma, 20 with primary open angle glaucoma, 13 with pseudoexfoliation glaucoma, and 12 with ocular hypertension and 21 control subjects. All the study subjects had

bilateral involvement and one eye was selected randomly. It was found that the CCT was significantly higher in patients with ocular hypertension than in normal population or in individuals with normal tension glaucoma, open angle glaucoma or pseudoexfoliation glaucoma. No statistically significant difference was found to exist between the latter four groups. This study did not demonstrate a significant thinning of the central cornea in PEXG. [85]

Seydi Okumus et al. retrospectively analyzed 159 cases with pseudo exfoliation (115 cases with cataract and 44 cases without cataracts) and compared the CCT in terms of average keratometric values and axial length with that of 60 normal subjects. In their study, a statistically significant difference was found to exist in the CCT between the eyes with pseudoexfoliation and those of the healthy subjects. The CCT was thinner when compared with the normal subjects. However, no significant difference was noted in the keratometric values and axial length measurements between the 2 groups. [86]

Civcic et al. measured the central corneal thickness in 26 eyes with normal tension glaucoma, 18 eyes with pseudoexfoliation glaucoma, 14 eyes with ocular hypertension and 88 eyes with primary open angle glaucoma using an ultrasonic pachymeter and compared them with 38 eyes without glaucoma which served as control group. They found that the CCT was significantly

thinner in the eyes with normal tension glaucoma and significantly thicker in the eyes with ocular hypertension. However, there was no significant variation in the CCT in eyes with POAG and PEXG when compared with the control group. [87]

Georgios Kitsos et al. evaluated the CCT in 32 patients with bilateral PEXG, 55patients with bilateral POAG, 35 patients with PXS but without glaucoma, and 57 normal subjects without PXS using an ultrasound pachymetry. The CCT was found to be significantly thinner in the patients with PEXG. No significant variation was observed in the CCT between the patients with POAG, PXS and the healthy subjects. [88]

Emine Sen et al. studied the CCT in 120 subjects with POAG, 62 subjects with PEXG, 51 subjects with NTG and 53 cases of ocular hypertension and 50 healthy subjects using an ultrasound bio pachymeter. They found that the CCT was significantly thinner in subjects with NTG and significantly thicker in subjects with OHT. They also found out that no significant difference existed in the CCT of the subjects with POAG and PEXG when compared with the control group. They concluded that the measurement of CCT is mandatory for monitoring glaucoma cases or glaucoma suspects for proper diagnosis and follow-up of the disease. [89]

Stefaniotou et al. evaluated the CCT and corneal endothelium in 48 patients with unilateral or bilateral pseudo exfoliation and compared the values against 48 normal subjects with no other ocular disease other than cataract. A significant decrease in the corneal endothelial cell density was observed along with a higher rate of polymegathism in the individuals with PXS when compared with the individuals without PXS. The CCT was found to be significantly thicker in the former group than the latter. However in patients with unilateral PXS, there was no significant difference in the CCT as well as the corneal endothelium between the eye with PXS and the fellow eye. [90]

Arnarsson et al., in their study entitled 'Pseudo exfoliation in the Reykjavik eye study' recruited 1045 subjects and evaluated the age and sex related prevalence of pseudo exfoliation in them. They also assessed other parameters like IOP, CCT, anterior chamber depth, lens thickness, optic disc diameter, the disc area and the cup disc ratio and compared them between the eyes with and without pseudo exfoliation. The CCT was measured using Scheimflug photography in 952 eyes, out of which 65 subjects had PEXF and 753 did not have PEXF. 134 subjects were excluded because the diagnosis of PEXF was not certain as very early exfoliative changes could not be ruled out. In this study, they did not find any significant difference in the CCT between the two groups after age and sex adjustments. [91]

Detorakis et al studied the central corneal mechanical sensitivity and the central corneal thickness in 40 patients with unilateral and bilateral pseudo exfoliation using the Cochet & Bonnet aesthesiometer & ultrasound pachymeter respectively and compared the same with 38 normal subjects without pseudoexfoliation. They inferred that the central corneal mechanical sensitivity was reduced in the eyes with PEXF and attributed it to decreased Schirmer's test values & tear film BUT. However, they observed that there was no significant difference in the CCT between the two groups. [31]

Aghaian E et al., in a retrospective study, analyzed the CCT in different subgroups of the Asian population such as the Japanese, Hispanics, Chinese, Caucasians, Filipinos and African Americans and measured the outcomes in terms of its correlation with race, age, gender, the presence or absence of glaucoma, the type of glaucoma, history of intra ocular surgery etc. 801 patients were included in the study out of which 600 patients were with glaucoma of any type and 201 patients were without glaucoma. They found out that the CCT was significantly variable among the different populations. It was also made out that OHT patients had thicker corneas and elderly patients and those with POAG, PEXG, CACG and NTG had significantly thinner corneas when compared with the normal population. [46]

Yeshigeta Gelaw et al., in a multicentric cross sectional study, measured & analyzed the CCT & IOP in 199 patients with glaucoma. They found that a statistically significant linear relationship existed between CCT and IOP. Among the study population, patients with OHT and PEXG had thicker corneas and higher IOPs when compared with NTG and POAG patients. [92]

Yagci et al. measured the IOP using GAT and CCT using ultrasonic pachymeter in 26 cases of POAG, 25 cases of PEXG and 24 cases with OHT and compared the values with 50 normal subjects. Results analyzed showed a significantly higher CCT in the subjects with OHT. Though the CCT was relatively thinner in cases with PEXG than those with POAG and the normal subjects, the difference between the three groups (POAG, PEXG and normal subjects) were statistically insignificant. [93]

Bechmann et al. measured the central corneal thickness in 167 individuals. Out of them 20 had primary open angle glaucoma , 42 had normal tension glaucoma, 22 had ocular hypertension, 10 had primary angle closure glaucoma, 24 had pseudoexfoliation glaucoma , 13 had Pigmentary glaucoma, and remaining 36 were without glaucoma and were designated as controls. Their study revealed that the CCT was significantly thicker in patients with OHT than that of the control group. However, in the other groups such as NTG, PEXG and POAG, the CCT was significantly lesser than that of the control

group. No statistically significant difference was found between the PIG group and the controls. [94]

The fact that CCT is thinner in PEXG has been demonstrated in most of the above studies. [16, 46, 81, 88, 94] However, the same has been contradicted by few other studies [80, 84, 85, 87, 89, 93] too as no significant difference in the CCT was made between PEXG subjects and the normal subjects. Another study [92] pointed out that the CCT was thicker in cases with PEXG. All these studies, except a few [91], have limitations such as a very small sample size. Moreover, instead of a single standard technique, different studies have employed different techniques such as ultrasound pachymeter, OCT, OLCR, Scheimflug photography, specular microscope, etc.

As most of these studies were cross sectional and retrospective, they were not able to document the CCT values of the subjects with PEXG prior to the development of glaucoma. There are certain prospective studies that have demonstrated the increased risk of developing glaucoma in PXS compared to those without PXS. [40] However, such studies too have not incorporated the CCT measurements in them.

However, few cross sectional studies have been done on the CCT in PXS (PEXF without glaucoma) and most of the studies [17, 78, 79, 80, 86] support the fact

that the CCT is significantly thinner in eyes with PXS than in normal eyes without PXS, except few studies [31, 82, 91] that have demonstrated no significant difference in the CCT between the two groups.

The role of CCT in terms of its correlation with IOP as an important tool in the diagnosis, classification, management and follow up of glaucoma has been well emphasized by various studies.[5,6] Different studies have documented that CCT differs in different types of glaucoma and the IOP readings must be adjusted accordingly not only to ensure a correct diagnosis of glaucoma but also to determine the exact target pressure to be achieved and to ensure during follow- ups if the IOP has been really controlled to the desired level.

Various studies have proved that individuals with PXS are at a higher risk of developing glaucoma than those without PXS. [38,39,40] PEXG has a worse prognosis than POAG as most of the patients present with significantly severe optic nerve damage at the time of diagnosis with a worse visual field damage. The response to medical management is also poor and there is increased necessity for surgical intervention. [41] Most studies attribute the severity of glaucomatous damage in PEXG to the delay in diagnosis due to underestimation of the IOP by GAT because of thinner corneas and failure to

achieve the actually desired target IOP. In most cases, the disease progresses with an apparently controlled IOP. As thinner CCT itself serves as an additional risk factor for the development of glaucoma in PXS, CCT measurement is mandatory in all PXS patients to facilitate early detection of glaucoma, determination of the exact target pressure to be achieved and monitoring the disease progression and the response to treatment.

AIM:

To compare the central corneal thickness in individuals with pseudo exfoliation syndrome and without pseudo exfoliation syndrome.

OBJECTIVES:

- To measure the central corneal thickness in individuals with pseudo exfoliation syndrome and compare it with that of individuals without pseudo exfoliation syndrome.
- To compare the central corneal thickness in the eyes with pseudo exfoliation with their fellow eyes without pseudo exfoliation, in individuals with unilateral pseudo exfoliation syndrome.
- To determine the influence of age and sex on central corneal thickness in both the study & control groups.
- To evaluate the differences in intra ocular pressure between the study and control groups, before and after adjustment for CCT.
- To emphasize the necessity for measuring the central corneal thickness in eyes with Pseudo exfoliation syndrome.

MATERIALS & METHODS

This is a hospital based, cross sectional study undertaken at the Department of Ophthalmology, Coimbatore Medical College and Hospital, Coimbatore.

The study period was about 12 months extending from November 2012 to October 2013.

Patients attending the Ophthalmology Out Patient Department & those admitted in the ward were selected on the basis of the following criteria:

INCLUSION CRITERIA:

- Adult patients of age 50 years & above with or without cataract.

EXCLUSION CRITERIA:

Patients with the following conditions in any one or both the eyes were excluded from the study:

- Any corneal pathology
- Uveitis
- Ocular trauma
- History of glaucoma
- IOP > 21 mm Hg

- Field defects and fundus changes suggestive of glaucoma
- History of contact lens wear
- History of previous intra ocular surgeries.
- Diabetes mellitus

All the patients aged 50 years and above were selected on the basis of the above criteria and written consent was obtained. A detailed history taking was done in order to rule out history of ocular trauma, intra ocular surgeries, contact lens wear, history of glaucoma, uveitis, corneal and other ocular diseases and history of medications for the same. History of diabetes mellitus and treatment for the same were ruled out.

A slit lamp examination was done in all patients with undilated pupil to rule out corneal pathologies like keratitis, corneal opacity, edema, scar, dystrophy, ectasia, and degeneration. Uveitis, conjunctival blebs, aphakia, pseudophakia were also ruled out. All were examined for the presence or absence of pseudo exfoliation. Pseudo exfoliation was diagnosed by the presence of white flakes or fibrillo granular material on the pupillary margin. A slit lamp examination was done again with a dilated pupil to detect presence of PEXF on anterior lens capsule. The presence or absence of cataract and if present the grading of cataract was noted.

Blood samples were taken to measure the blood glucose and urine analysis was done. Only those individuals with blood glucose values less than 140 mg% and nil urine sugar were included in the study.

Visual acuity, visual field examination, gonioscopy and refraction were done for all patients. A detailed fundus examination was done to rule out glaucomatous changes. The IOP was measured using GAT. CCT was measured using ultrasonic pachymetry (PAC SCAN 300 P). The details of the patient, along with the IOP of both eyes were fed into the pachymeter. After instillation of 0.5% proparacaine, the patients were made to sit upright looking straight ahead. The tip of the hand held pachymeter probe was placed perpendicularly on the cornea and centered over the undilated pupil. An average of five consecutive readings were recorded. The predesigned software incorporated in the pachymeter auto adjusted the IOP according to the CCT and gave the true IOP along with the mean CCT value.

The patients with CCT adjusted IOP > 21 mm Hg, those with fields and fundus changes suggestive of glaucoma were excluded from the study.

The patients who fulfilled all the above criteria were designated as study subjects based on the presence of PEXF on the pupillary margin and/or the anterior lens capsule. Those without PEXF were designated as controls. A total

of 100 subjects without PEXF and 50 subjects with PEXF were included in the study. Their IOP and CCT values were tabulated and analyzed for statistical significance.

The data analysis and interpretation was done using SPSS 16 version. The mean, standard deviation, standard error of mean, degree of freedom, 2-tailed significance and 95 % confidence interval were calculated. Independent t test, one way analysis of variance (ANOVA) and Pearson's correlation were used for analysis of the results.

Figure11. Technique of Applanation tonometry

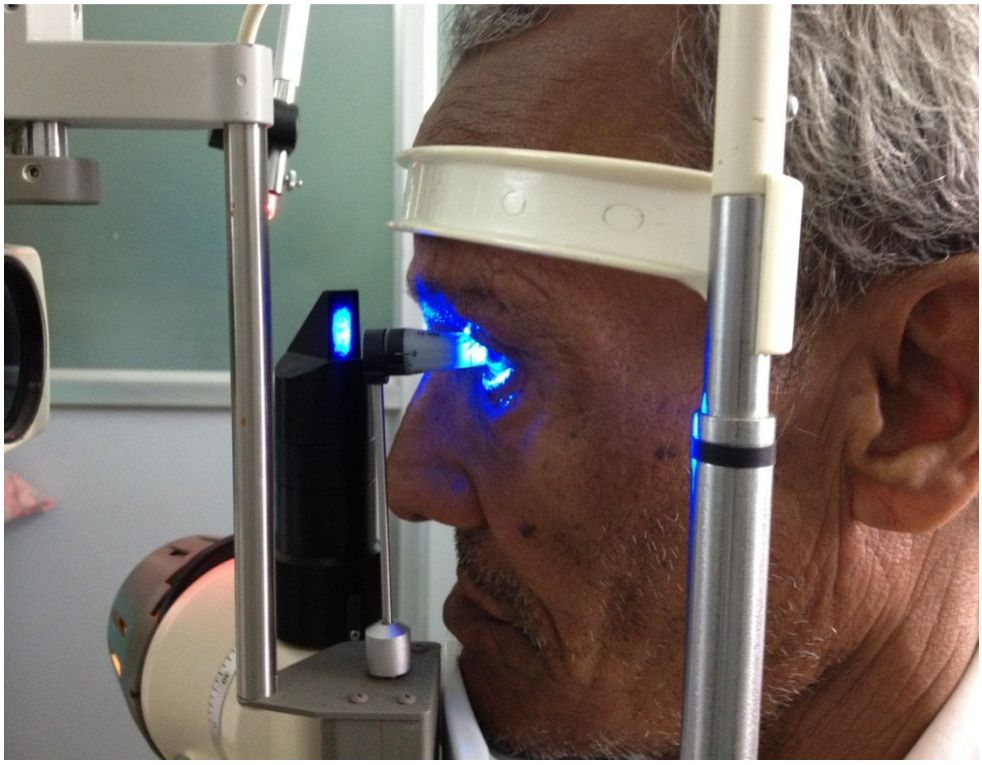


Figure 12. Technique of Ultrasound Pachymetry

RESULTS AND OBSERVATION

Among the 100 subjects of the control group, 40% were males and 60 % were females. In the 50 subjects of the PEXF group, 54% were males and 46 % were females.

Table 1. Gender distribution in Control and PEXF group

Gender	Control Group		PEXF Group		Total	
	No. of patients	%	No. of patients	%	No. of patients	%
Male	40	40	27	54	67	44.7
Female	60	60	23	46	83	55.3
Total	100	100	50	100	150	100

The above data shows that within the PEXF group, the number of males were higher (54 %) than females (46%)

Chart 1. Gender distribution in Control and PEXF group

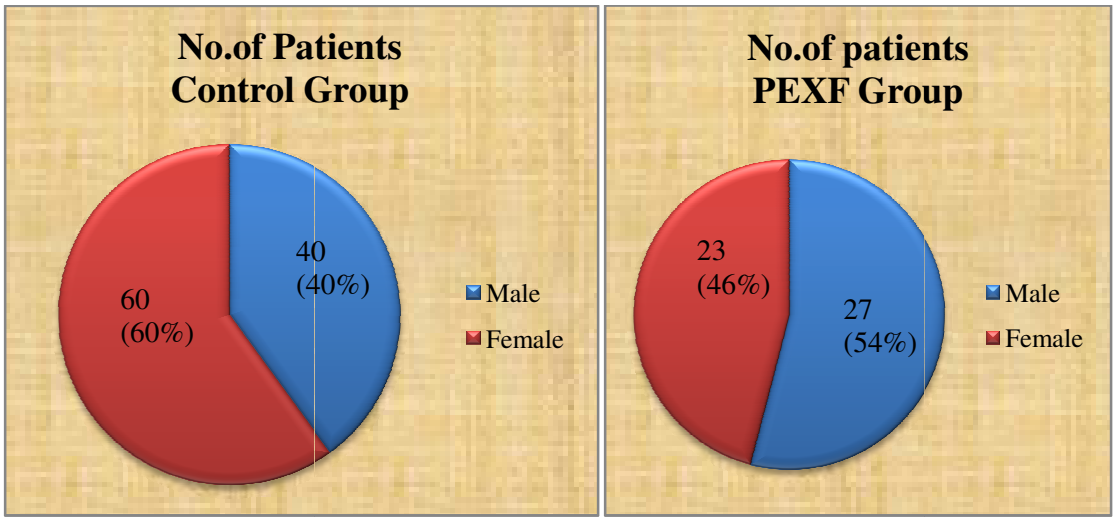


Table 2. Overall gender-wise distribution of PEXF

Gender	Total	PEXF Group		Control Group	
		No. of patients	Percentage	No. of patients	Percentage
Male	67	27	40.3%	40	59.7%
Female	83	23	27.7%	60	72.3%

On estimating the overall gender distribution also, the distribution of PEXF was higher in males (40.3%) than in females (27.7%)

Chart 2. Overall gender-wise distribution of PEXF

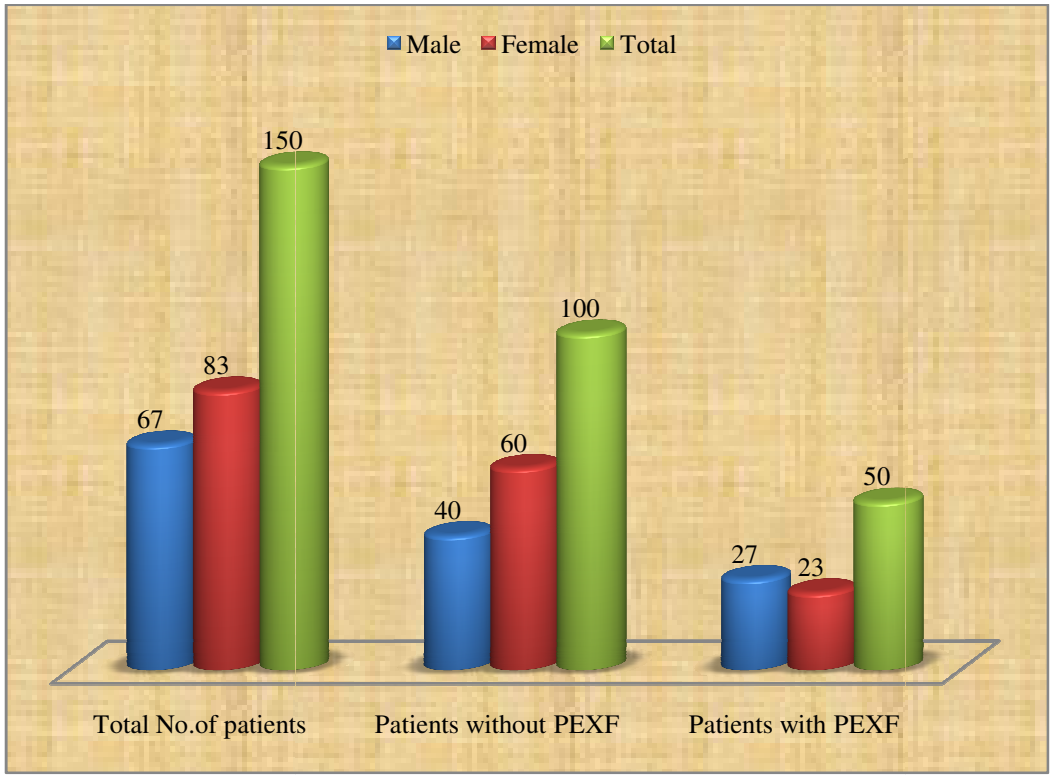


Table 3. Age distribution in Control and PEXF group

Age	Control Group		PEXF Group		Total	
	No. of patients	%	No. of patients	%	No. of patients	%
50-59	30	30%	10	20%	40	26.7%
60-69	48	48%	18	36%	66	44%
70-79	20	20%	19	38%	39	26%
80 &above	2	2%	3	6%	5	3.3%
Total	100	100%	50	100%	150	100%

The above table shows that most of the patients in the control group belonged to the age group of 60-69years (48%) whereas most of the patients in the PEXF group were in the age group of 70-79(38 %) years and 60-69 (36%) years. Thus this table shows that the number of patients in the PEXF group were maximum in the age group of 70-79 years (38%)

Chart 3. Age distribution in Control and PEXF group

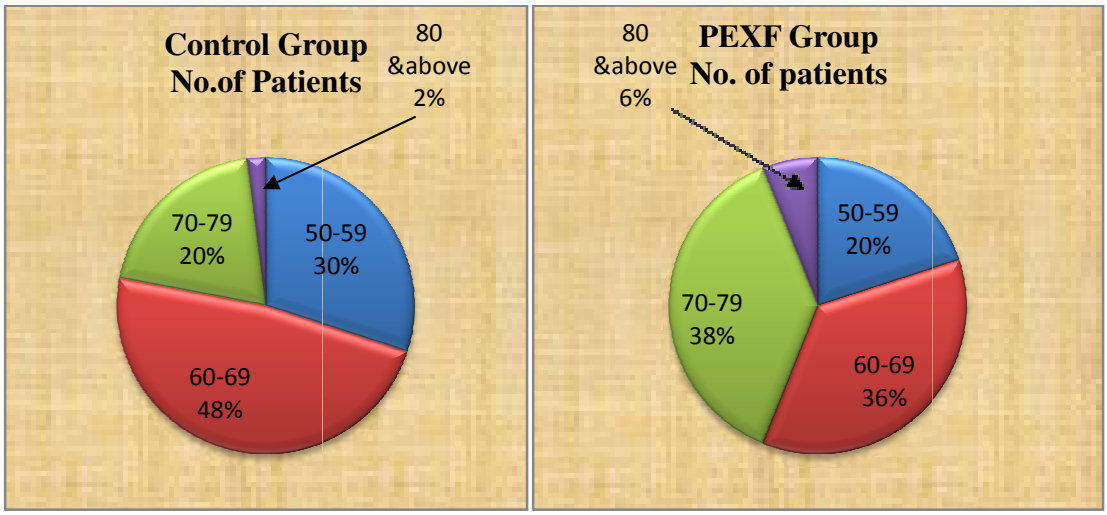


Table 4. Overall age-wise distribution of PEXF

Age (Years)	Total	With PEXF		Without PEXF	
		No. of patients	Percentage	No. of patients	Percentage
50-59	40	10	25%	30	75%
60-69	66	18	27.3%	48	72.3%
70-79	39	19	48.7%	20	51.3%
80 & above	5	3	60%	2	40%
Total	150	50	-	100	-

The above table shows that distribution of PEXF is maximum in those aged > 80 years(60%), followed by 48.7 % in those between 70 to 79 years and 27.3 % in those aged 60-69% years and least in the <60 years age group.

Chart 4. Overall age-wise distribution of PEXF

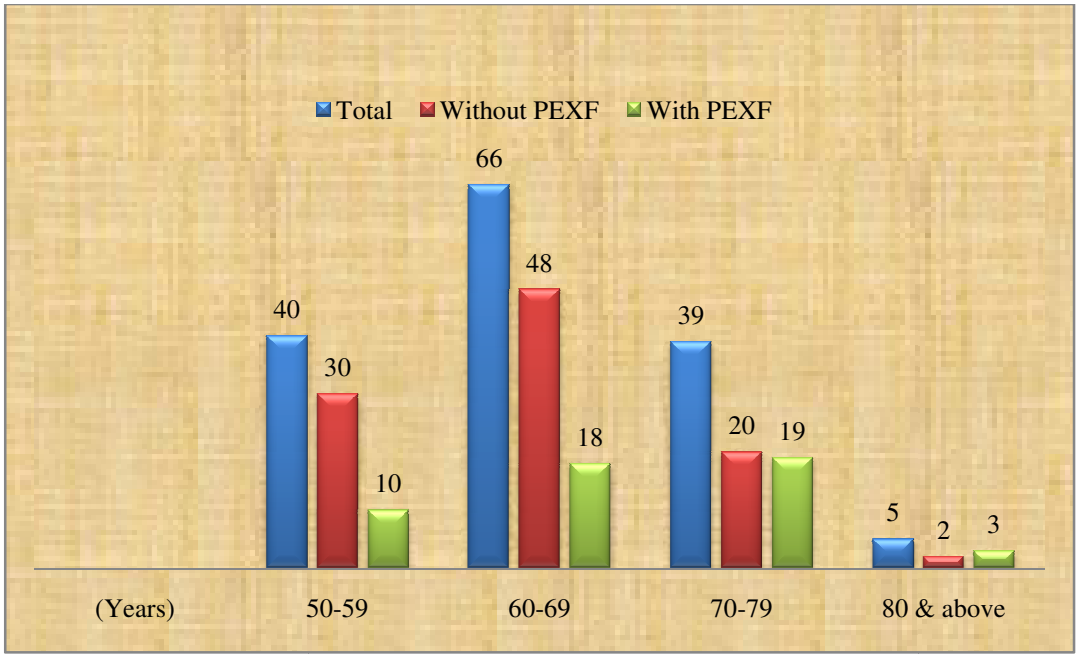


Table 5. Distribution of Laterality in PEXF group

	Bilateral PEXF	Unilateral PEXF	Unilateral PEXF		Total
			RE	LE	
No.of cases	30	20	9	11	50
Percentage	60%	40%	18%	22%	100%

The above table shows that in the PEXF group, 60% had bilateral PEXF and 40 % had unilateral PEXF (18 % in RE alone and 22% in LE alone)

Chart 5. Distribution of laterality in PEXF group

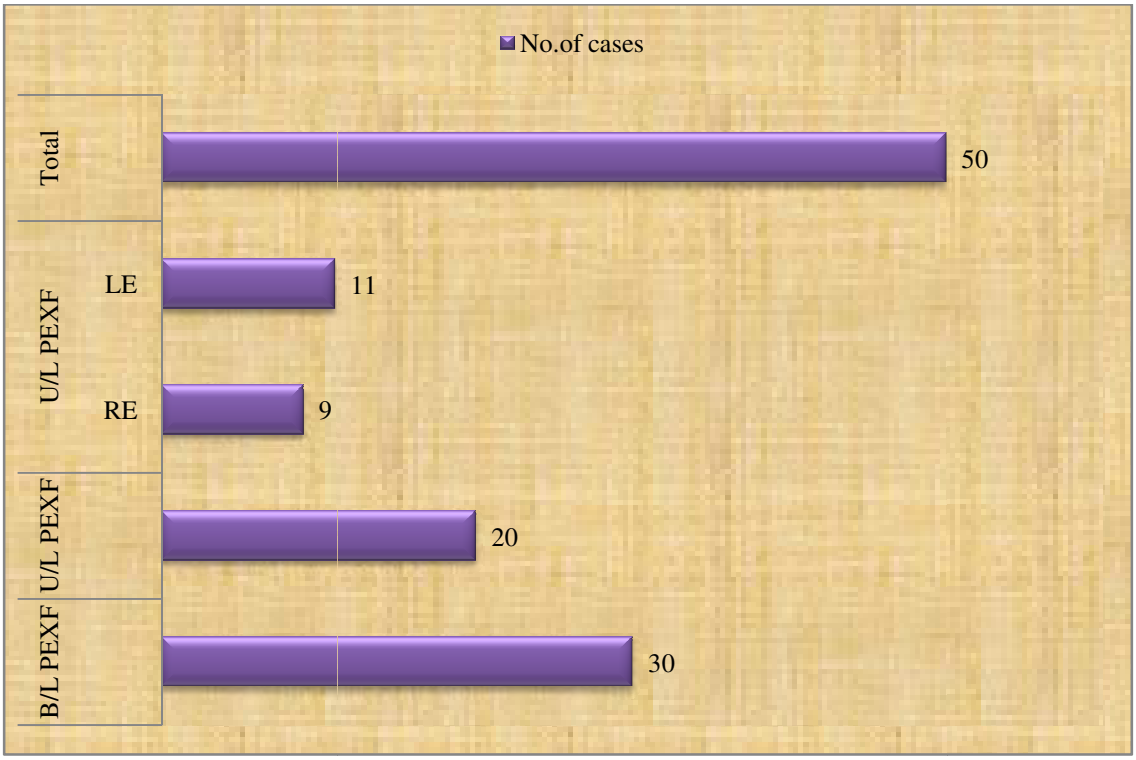


Table 6. Overall age-wise distribution of CCT

Age group (years)	Total No. of Patients	Mean CCT (in mm)
50-60	40	0.513
60-70	66	0.513
70-80	39	0.512
>80	5	0.476
Total	150	0.511

The above table shows that the mean CCT is almost same in all age groups except those aged 80 years and above, in whom there is marked decrease in CCT compared to the other three groups. However there was no significant statistical correlation between age and CCT (p value=0.352)

ANALYSIS OF VARIANCE

CCT	Sum of Squares	df	Mean Square	F	Sig.
Between groups	0.004	3	0.001	1.099	**0.352**
Within groups	0.170	144	0.001		
Total	0.174	147			

Chart 6. Overall age-wise distribution of CCT

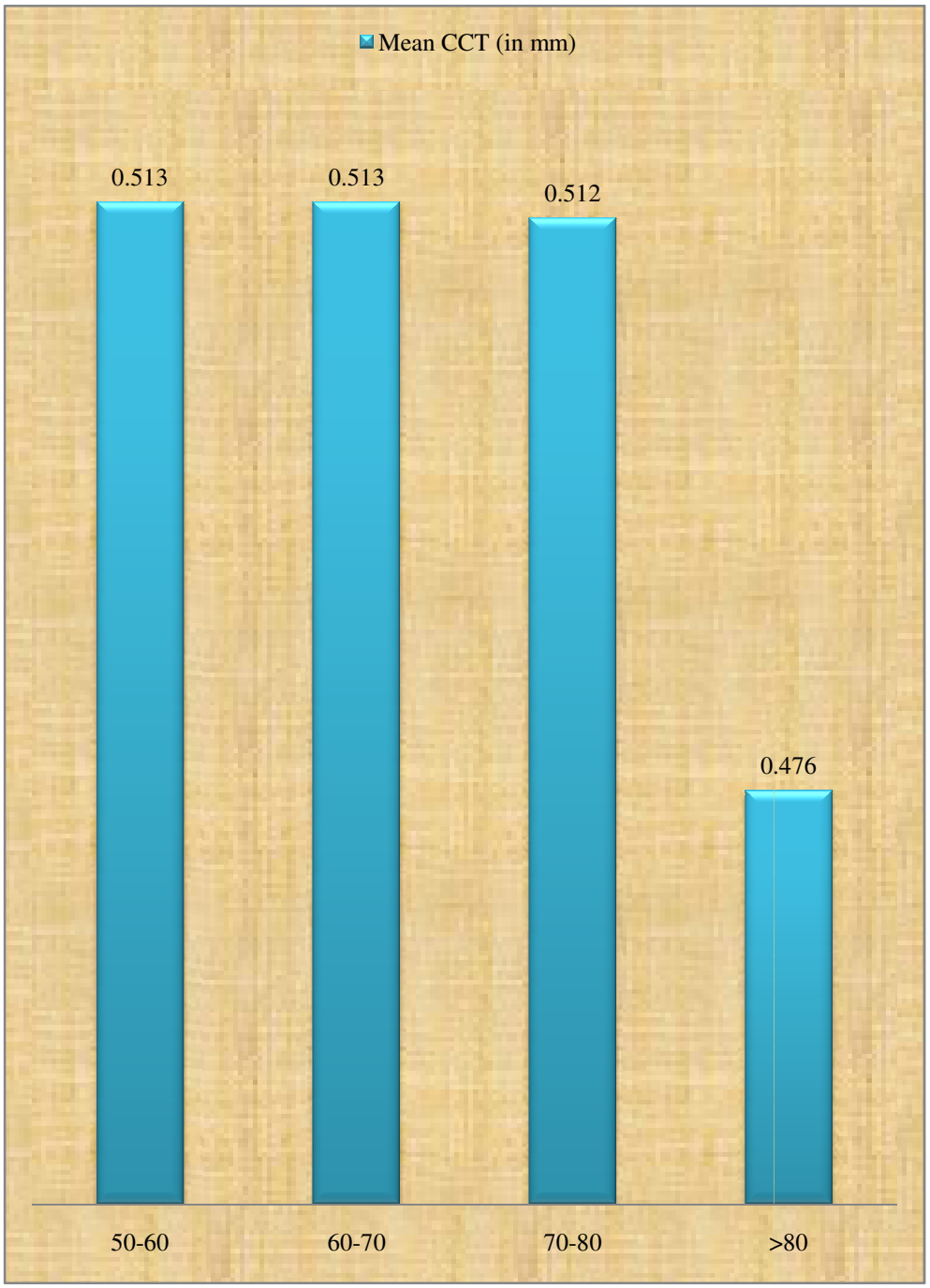


Table 7. Mean CCT in Control group

No of patients		Mean CCT (in mm)	Std deviation	Std error mean
100	**RE**	0.517	.03448	.00345
	LE	0.517	.03371	.00337

The above table shows that the mean CCT in the control group without PEXF is 0.517 $\pm$ 0.07 mm in BE. This also shows that there is no difference in the CCT value between both eyes.

Chart 7. Mean CCT in Control group

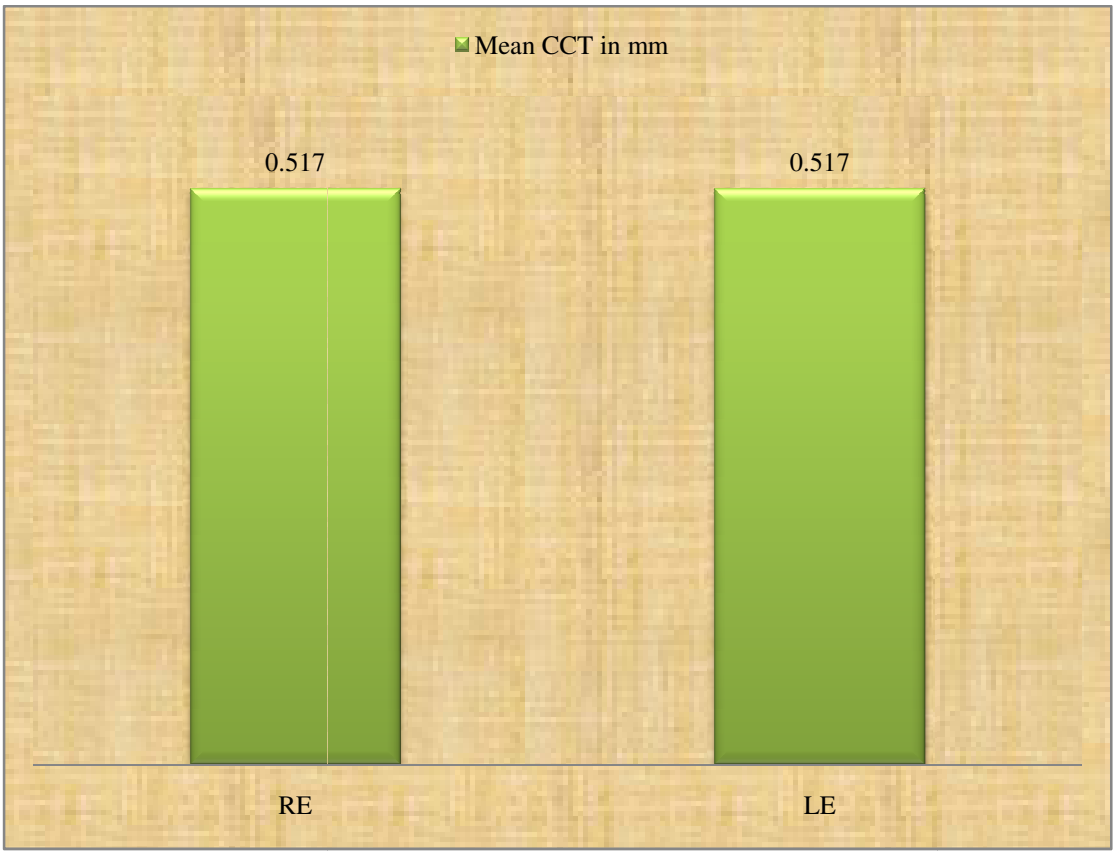
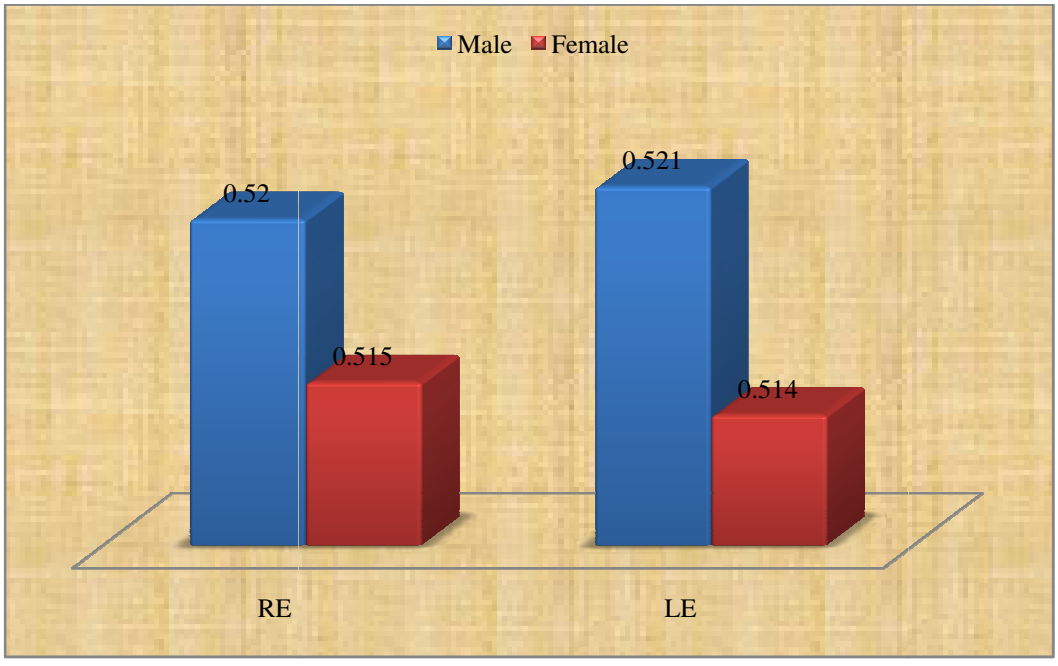


Table 8. Gender-wise distribution of CCT in control group

	Gender	No. of patients	Mean CCT (in mm)	Std deviation	Std error mean
RE	**Male**	40	0.520	0.03487	0.00551
	Female	60	0.515	0.3436	0.00444
LE	**Male**	40	0.521	0.3470	0.00549
	Female	60	0.514	0.03303	0.00426

The above table shows that the mean CCT in males is 0.520 $\pm$ 0.07 mm and 0.521 $\pm$ 0.07 mm in the RE and LE respectively. In females, it is 0.515 $\pm$ 0.07 mm in the RE and 0.514 $\pm$ 0.07 mm. There is no significant difference in CCT between both eyes in both genders.

Chart 8. Gender-wise distribution of CCT in control group (in mm)



Independent samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
RE									
Eq. variances assumed	.038	.845	**.716**	98	**0.476**	.00505	.00706	-.00895	.01905
Eq. variances not assumed			.714	82.876	0.477	.00505	.00708	-.00903	.01913
LE									
Eq. variances assumed	0.001	0.973	**1.008**	98	**0.316**	.00693	.00688	-.00672	.02059
Eq. variances not assumed			0.998	80.836	0.321	.00693	.00695	-.00689	.02076

The mean CCT is found to be slightly higher in males than that of females in both eyes. However, this difference is statistically insignificant (P value RE=0.476 LE=0.316).

Table 9. Mean CCT in PEXF group

No. of patients		No. of eyes	Mean CCT (in mm)	Std Deviation	Std error of mean
50	**RE**	39	0.501	0.03504	0.00496
	LE	41	0.500	0.03240	0.00458

The above table shows that the mean CCT in the PEXF group is 0.501 $\pm$ 0.07 mm in RE and 0.500 $\pm$ 0.06 mm in LE. This also shows that there is no difference in the CCT value between both eyes.

Chart 9. Mean CCT in PEXF group

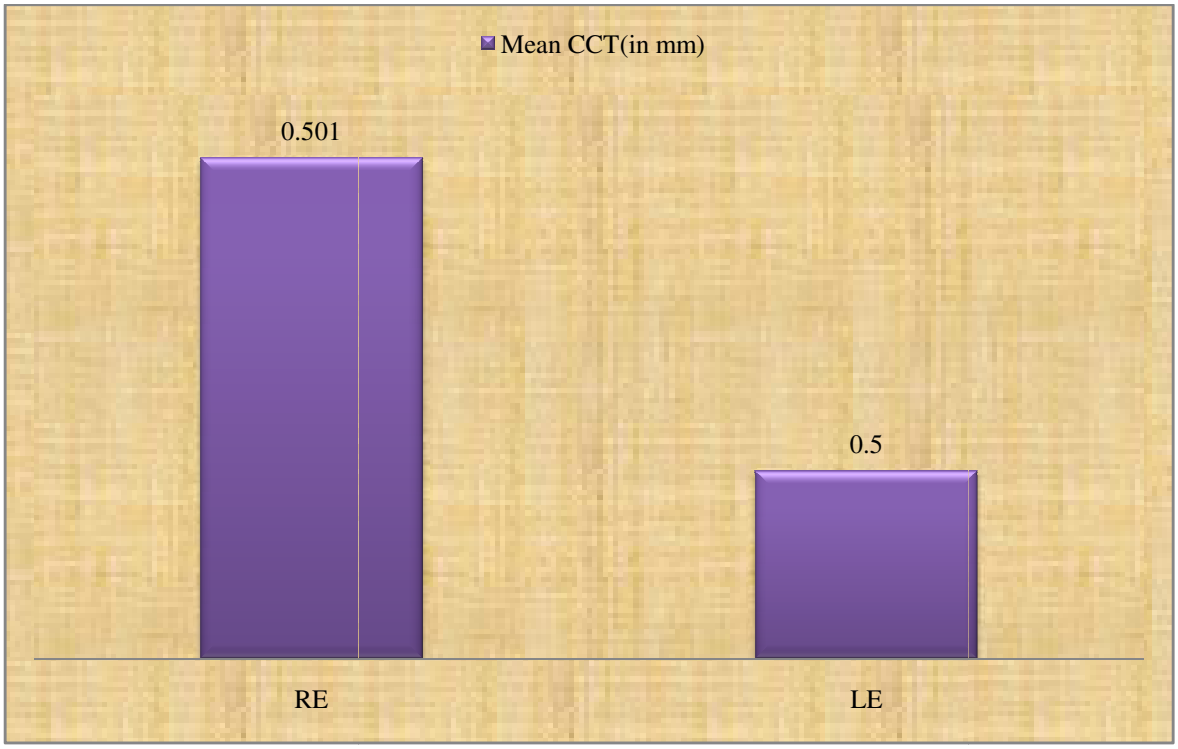


Table 10. Gender-wise distribution of CCT in PEXF group

	Gender	No. of patients	Mean CCT (in mm)	Std deviation	Std error mean
RE	**Male**	27	0.504	0.03551	0.00683
	Female	23	0.497	0.03489	0.00728
LE	**Male**	27	0.504	0.03170	0.00610
	Female	23	0.495	0.03327	0.00694

The above table shows that the mean CCT in males is 0.504 $\pm$ 0.07 mm RE and 0.504 $\pm$ 0.06 mm in LE. In females, it is 0.497 $\pm$ 0.07 mm in the RE and 0.495 $\pm$ 0.07 mm. There is no significant difference in CCT between both eyes in both genders.

Independent samples test

Mean CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error mean	95% Confidence Interval of the Difference	
								Lower	Upper
RE									
Eq. variances assumed	1.736	0.194	**0.693**	48	**0.492**	.00692	.01000	-.01317	.02702
Eq. variances not assumed			0.694	46.995	.491	.00692	.00998	-.01316	.02701
LE									
Eq. variances assumed	2.670	0.109	**0.965**	48	**0.339**	.00888	.00920	-.00962	.02738
Eq. variances not assumed			0.962	45.935	0.341	.00888	.00924	.00971	.02748

The mean CCT is found to be slightly higher in males than that of females in both eyes. However, this difference is statistically insignificant (P value RE=0.492 LE=0.339)

Chart 10. Gender wise distribution of CCT (in mm) in PEXF Group

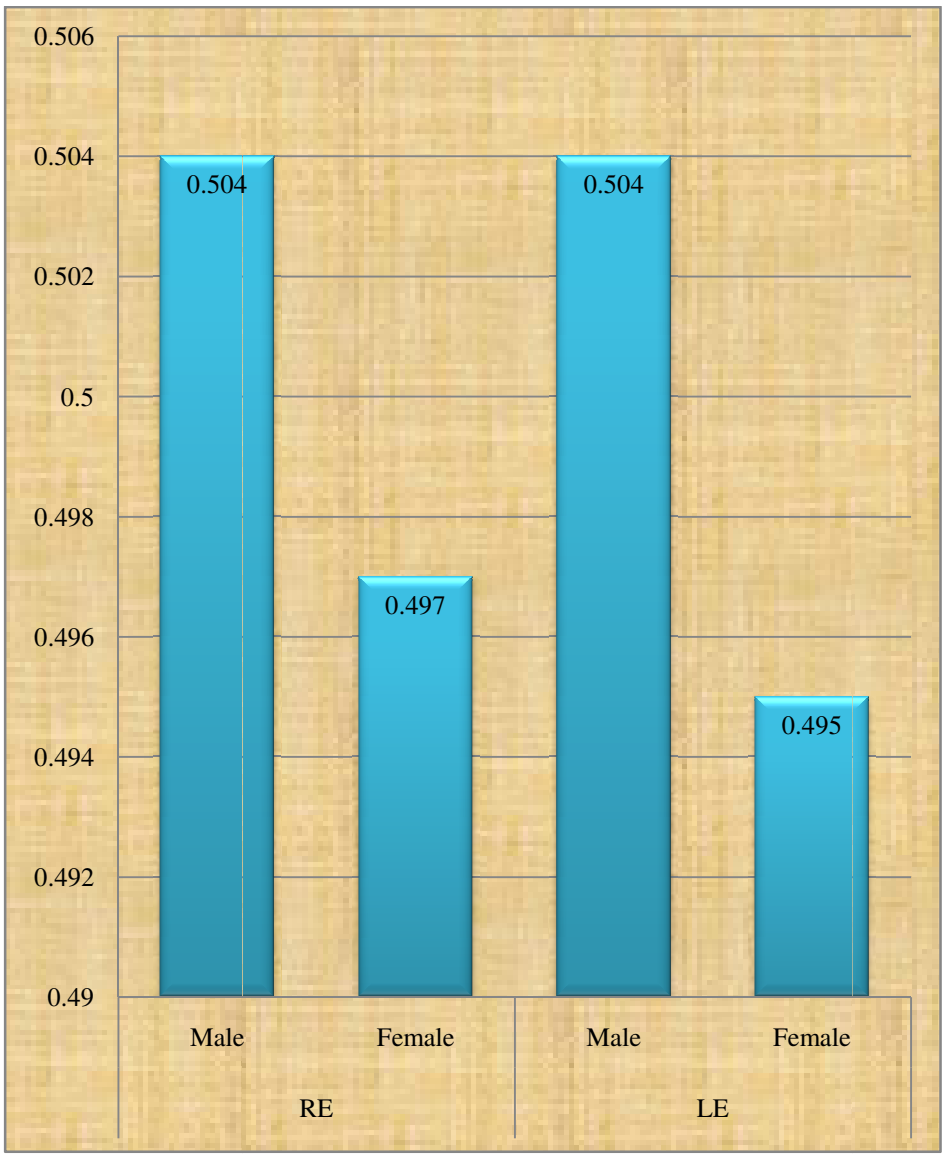
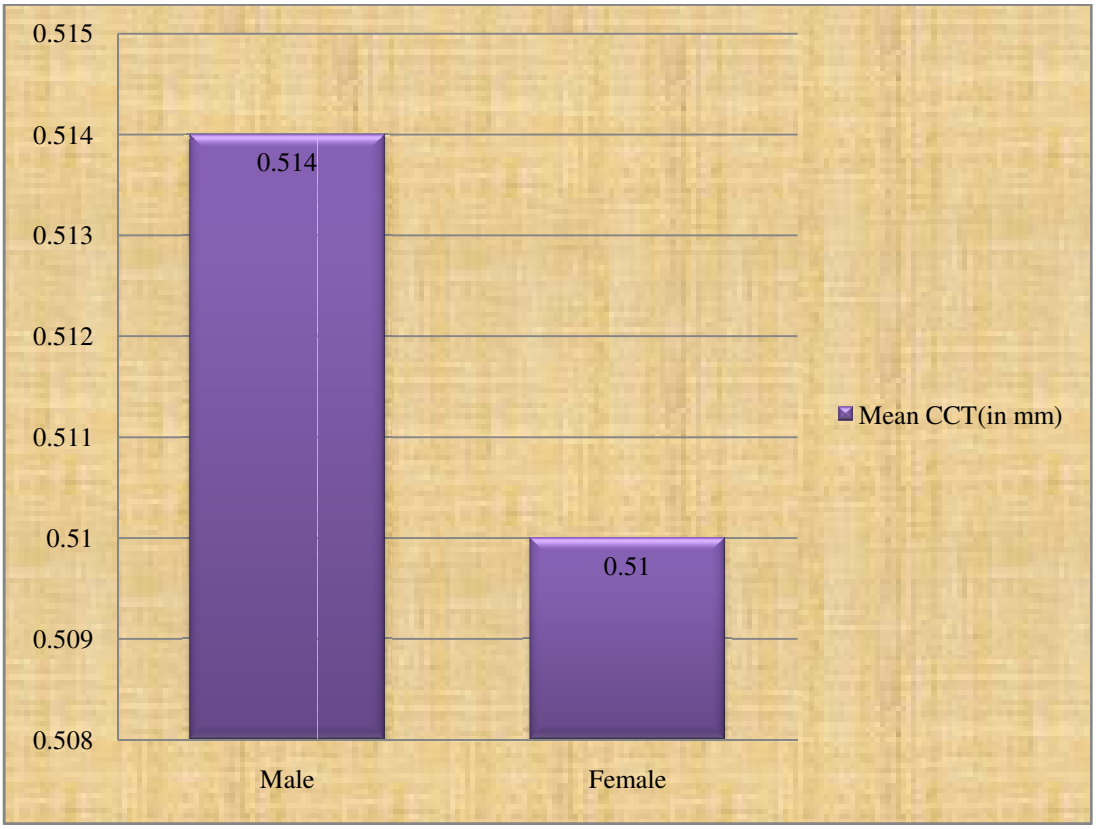


Table 11 Gender-wise distribution of CCT in overall population

Gender	No of patients	Mean CCT (in mm)	Std. Deviation	Std. Error Mean
Male	67	0.514	.0346875	.0042378
Female	83	0.510	.0343555	.0037710

Chart 11. Gender-wise distribution of CCT in overall population



The above table and column chart show that the CCT is slightly thinner in females when compared with males. However, the difference was statistically insignificant (P value= 0.436).

Independent samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
Eq. variances assumed	.438	.509	**0.782**	148	**0.436**	.004423	.005667	-.006769	.0156277
Eq. variances not assumed			0.781	140.83	0.436	.004429	.005673	-.006785	.0156440

Table 12.Comparison of CCT between both eyes in B/L PEXF group

No of patients		Mean CCT (in mm)	Std. Deviation	Std. Error Mean
30	**RE**	0.503	.03664	.00669
	LE	0.503	.03437	.00628

No variations were observed in the CCT of both the eyes of bilateral PEXF group.

Chart 12. Comparison of CCT between both eyes in B/L PEXF group

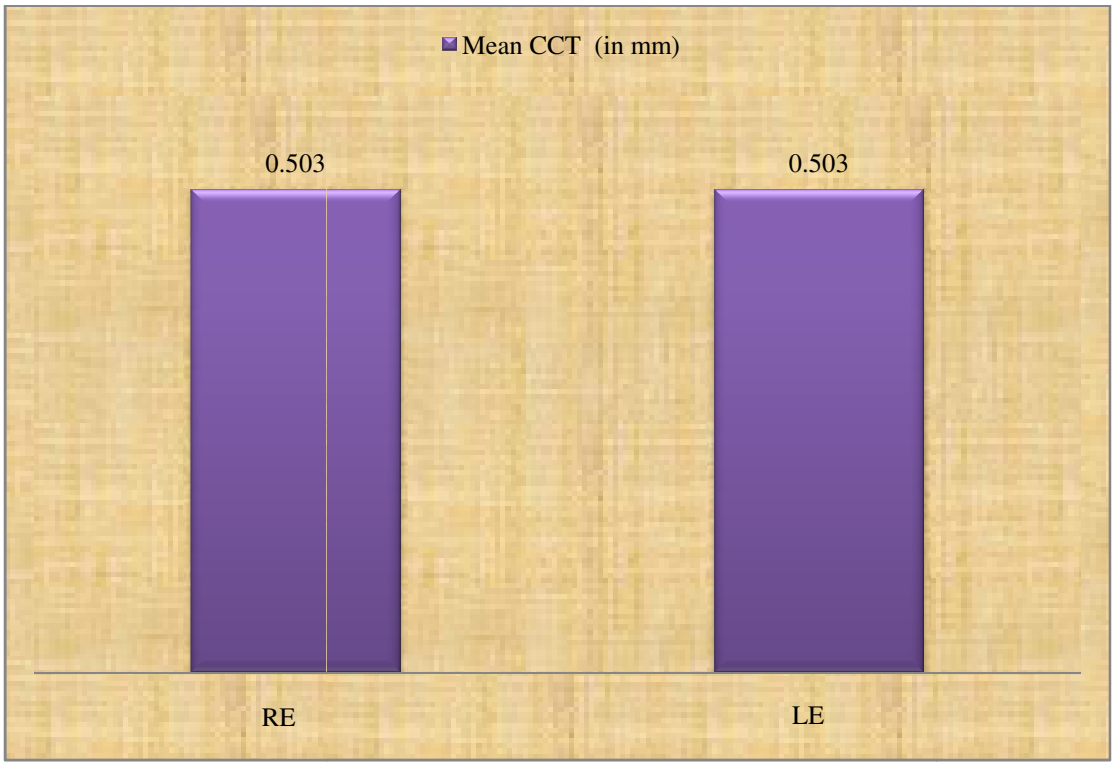


Table 13. Comparison of CCT between both eyes in U/L PEXF group

No of patients		Mean CCT (in mm)	Std. Deviation	Std. Error Mean
20	**Eye with PEXF**	0.494	.028644	.006405
	Eye without PEXF	0.499	.033630	.007520

Among the 20 cases with unilateral PEXF, the eye with PEXF had a thinner CCT (0.494 $\pm$ 0.06 mm) when compared with the fellow eye without PEXF (0.499 $\pm$ 0.07 mm). However, this difference was statistically insignificant (P value =0.644)

Independent samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
Eq.variances assumed	.176	.677	**-.466**	38	**.644**	-.0046	.00988	-.02459	.015397
Eq. variances not assumed			-.466	37.1	.644	-.0046	.00988	-.02461	.015413

Chart 13. Comparison of CCT (in mm) between both eyes in U/L PEXF group

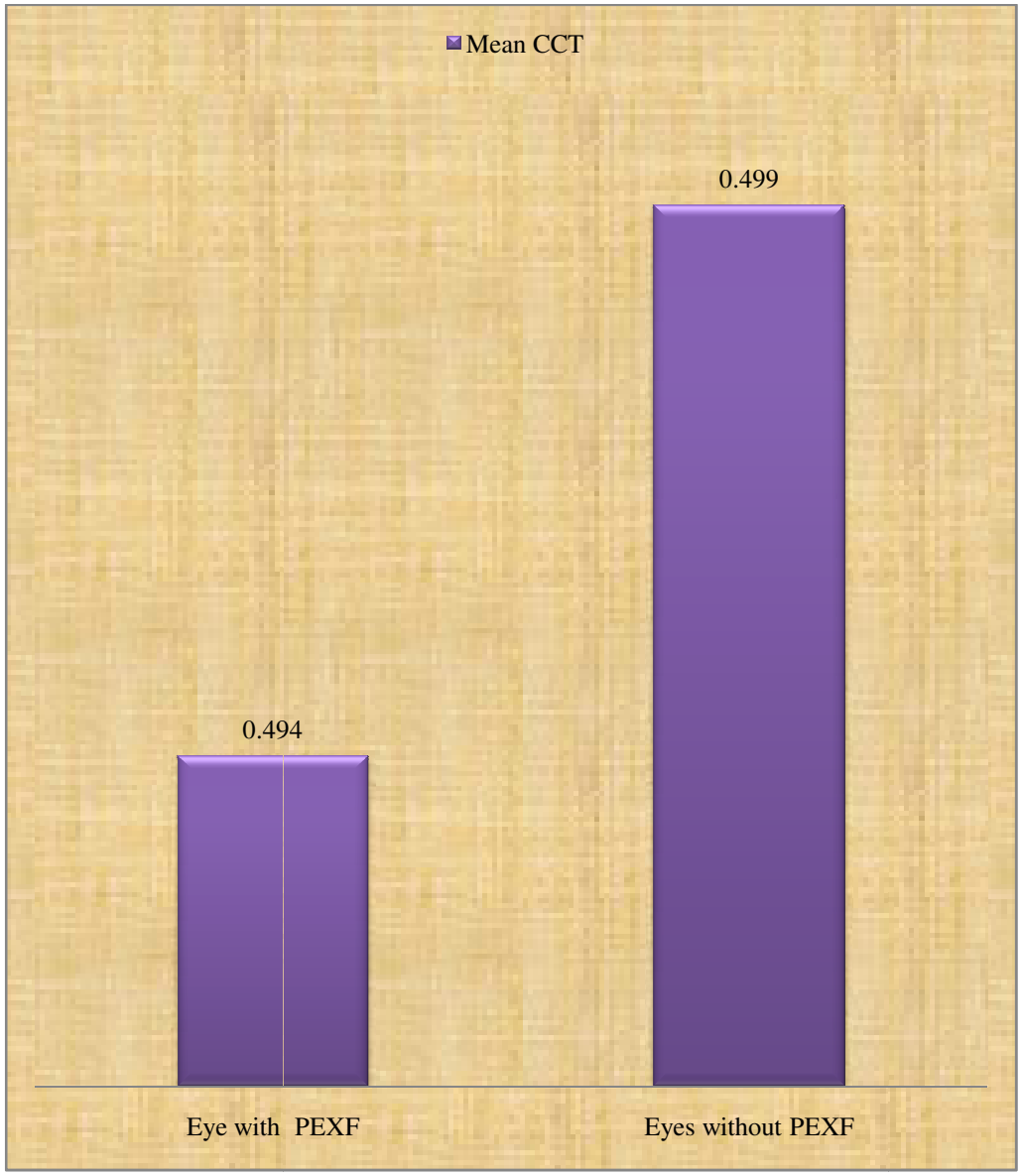


Table 14. Overall comparison of CCT between Control & PEXF group

GROUP	No. of patients	MEAN CCT(in mm)	
		RE	LE
Without PEXF	100	0.517	0.517
With PEXF	50	0.501	0.499

The above table shows that the CCT is significantly thinner in both the eyes of PEXF group than both the eyes in the control group without PEXF (P value RE= 0.008 LE = 0.003)

Independent samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
RE Eq.variance assumed	.683	.410	**2.685**	148	**0.008**	.01612	.00600	.00425	.02799
Eq.variances not assumed			2.670	96.709	0.009	.01612	.00604	.00414	.02810
LE Eq. variances assumed	1.104	.295	**2.984**	148	**0.003**	0.01720	0.00576	.00581	0.02859
Eq.variances not assumed			3.023	101.636	0.003	0.01720	0.00569	0.00592	0.02848

Chart 14. Mean CCT (in mm) in Control group and PEXF group

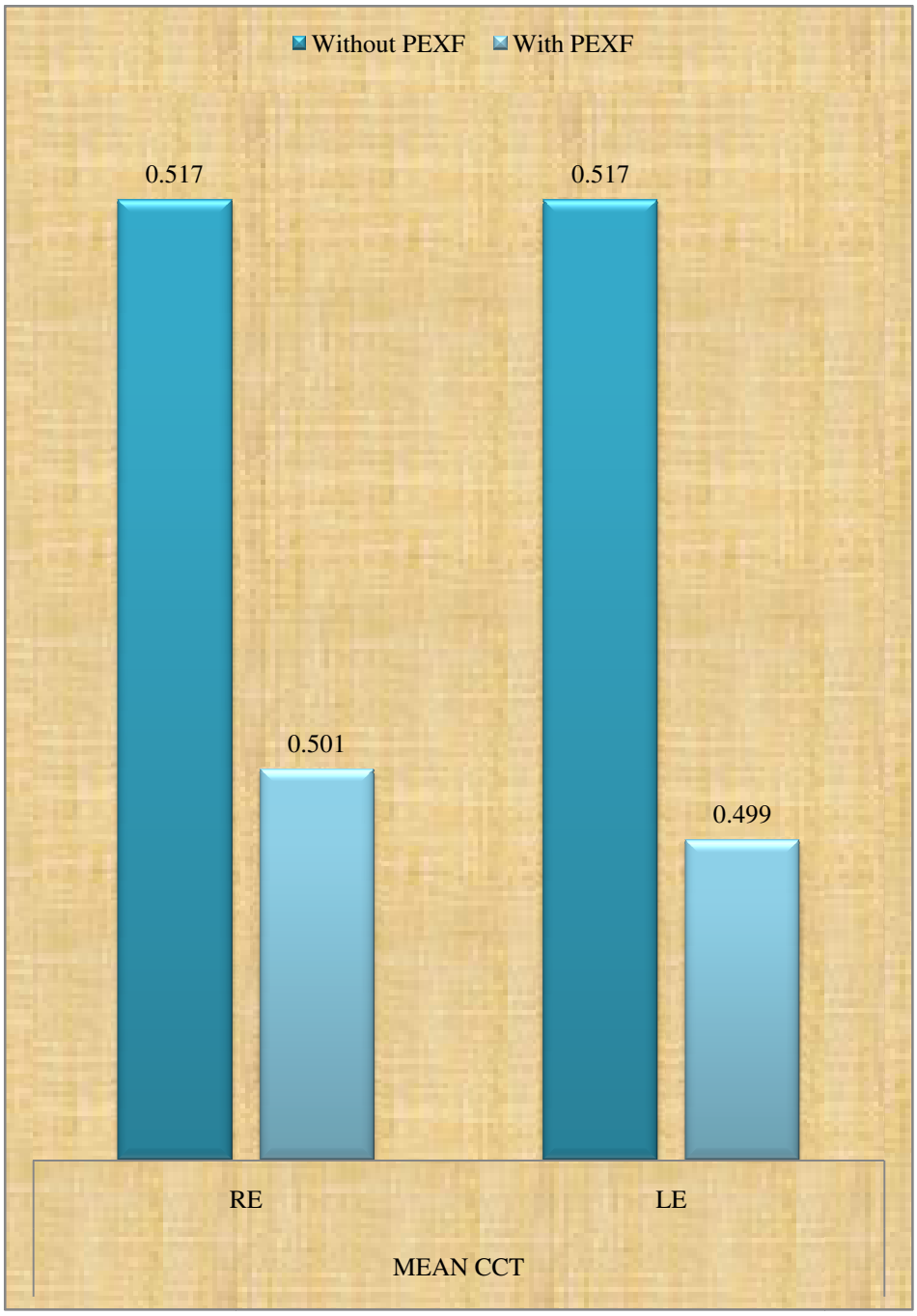


Table 15. Overall comparison of CCT in eyes with and without PEXF

Group	No. of patients	Mean CCT (in mm)	Std. Deviation	Std. Error Mean
Eyes with PEXF	80	0.501	.033767	.003775
Eyes without PEXF	220	0.515	.034318	.002314

Independent samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
Eq.variance assumed	1.880	.171	**-3.252**	298	**.001**	-.01451	.004462	-.02329	-.00573
Eq.variances not assumed			-3.277	142.248	.001	-.01451	.004428	-.02326	-.00576

Comparison of 80 eyes with PEXF in the PEXF group with the 220 eyes without PEXF (200 eyes in the control group and 20 eyes in the unilateral PEXF group) also showed a significant thinning in the eyes with PEXF (P value=0.001)

Chart 15. Overall comparison of CCT in eyes with and without PEXF

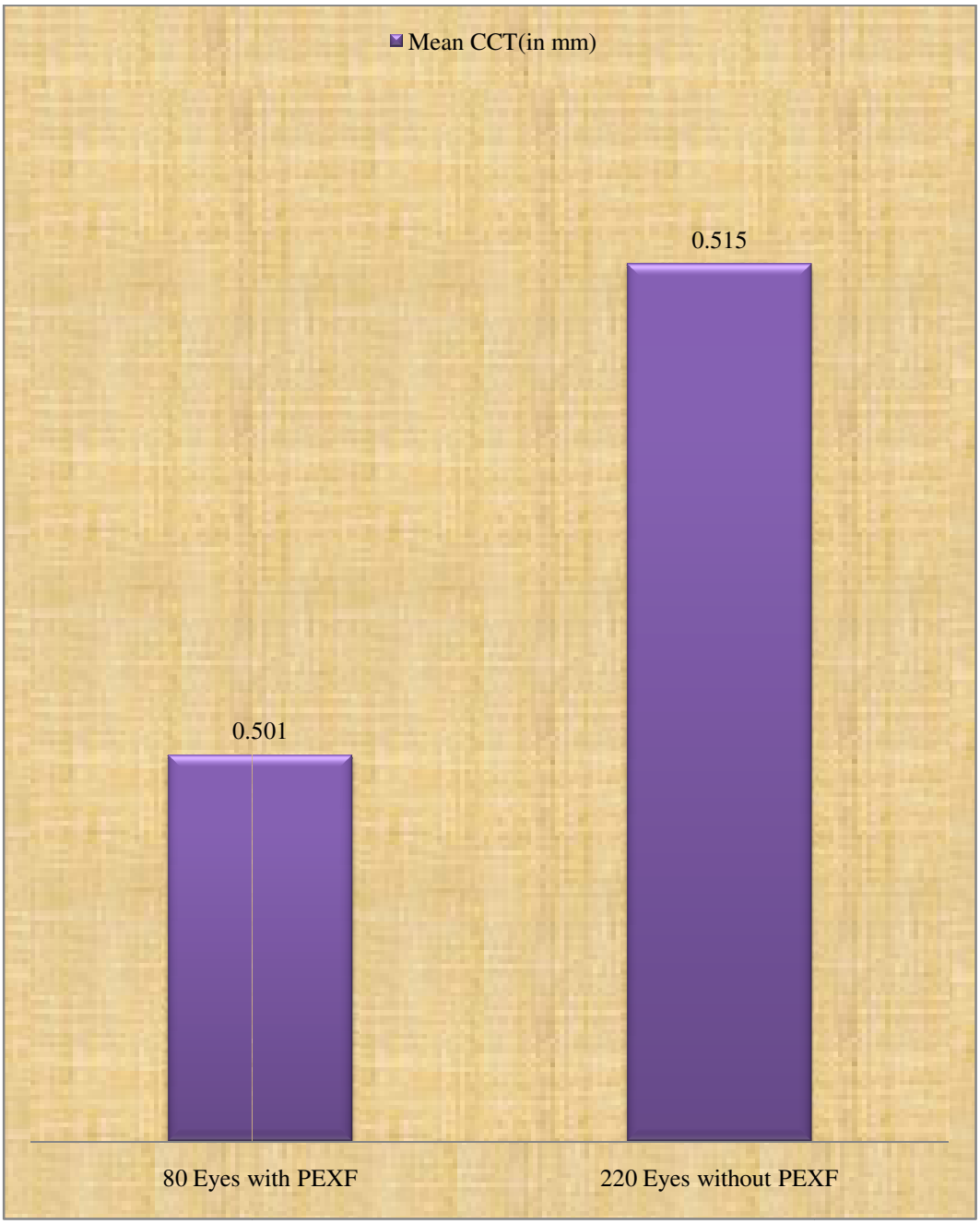


Table 16 Comparison of CCT between the eyes without PEXF in unilateral PEXF group and the Control group.

Group	No. of patients	Mean CCT (in mm)	Std. Deviation	Std. Error Mean
Eyes without PEXF in U/L PEXF group	20	0.499	.033630	.007520
Eyes without PEXF in Control group	200	0.517	.034010	.002405

The above table shows that the mean CCT is significantly thinner even in the eyes without PEXF in the unilateral PEXF group when compared with the normal group. (P value= 0.021)

Independent samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
Eq.variance assumed	0.636	.426	**-2.325**	218	**.021**	-.01853	.00797	-.034235	-.002825
Eq.variances not assumed			-2.347	23.062	.028	-.01853	.00790	-.034860	-.002200

Chart 16. Comparison of CCT between the eyes without PEXF in U/L PEXF group and the Control group.

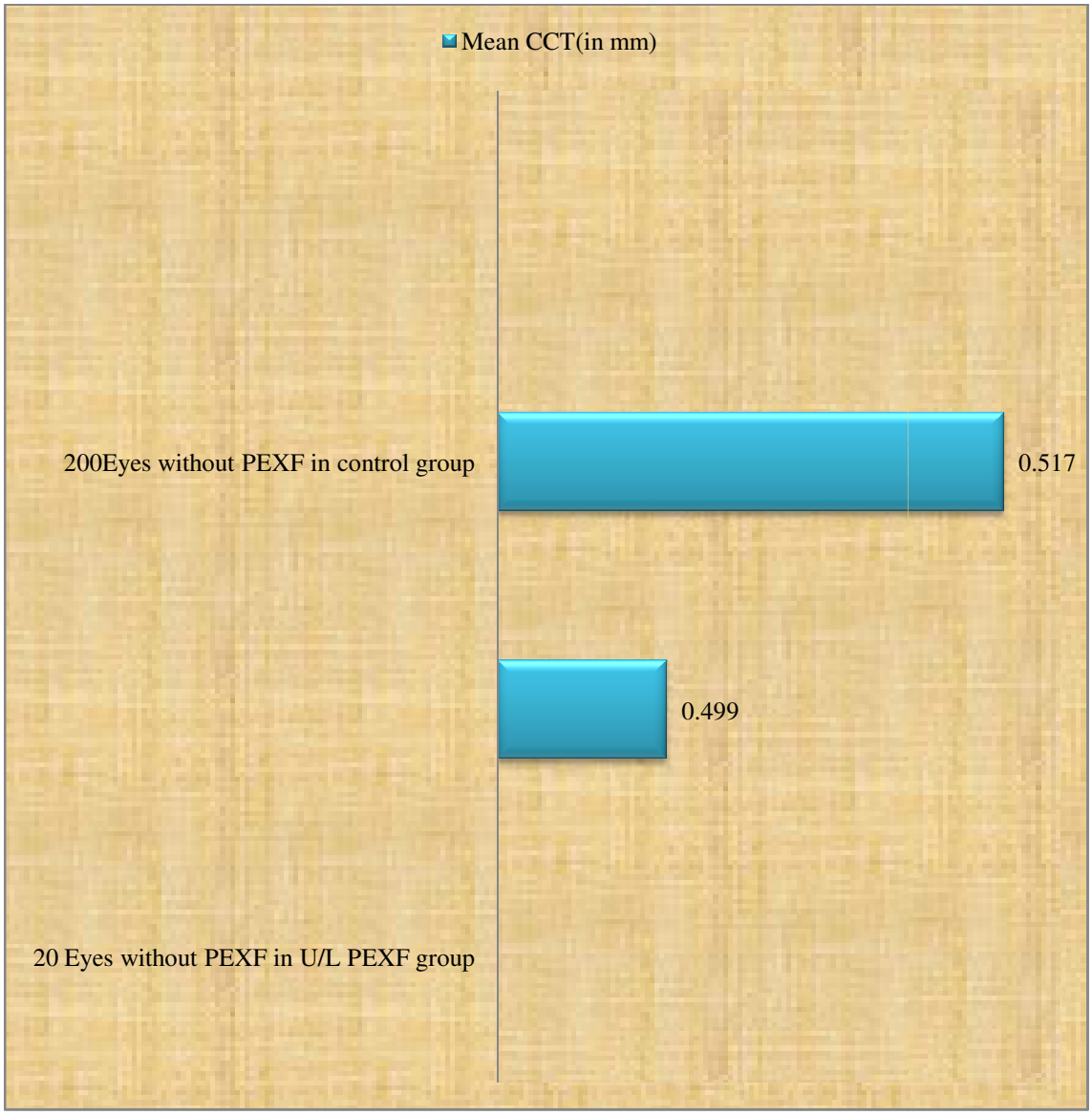


Table 17. Comparison of IOP between Control and PEXF group before CCT correction.

	Mean IOP before CCT correction(mm Hg)	
	Control group	**PEXF group**
RE	13.5	13.1
LE	13.2	13.2

The above table shows that the IOP is similar between the 2 groups in left eye. In right eye, the IOP is slightly higher in the control group than the PEXF group. However, the difference is statistically insignificant.

Chart 17. IOP in Control & PEXF group before CCT correction

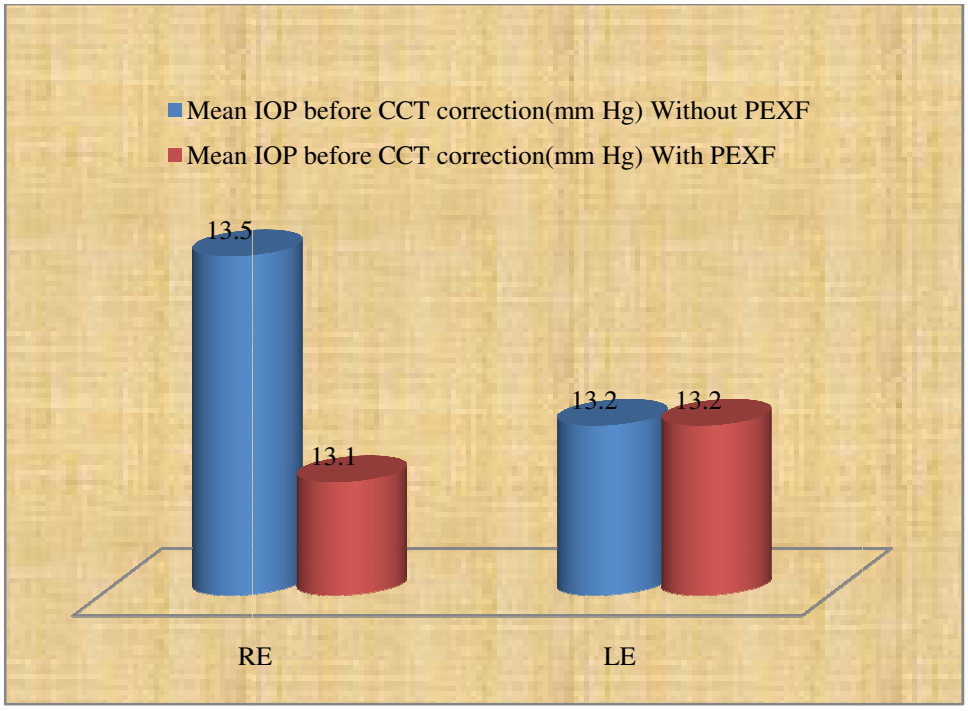
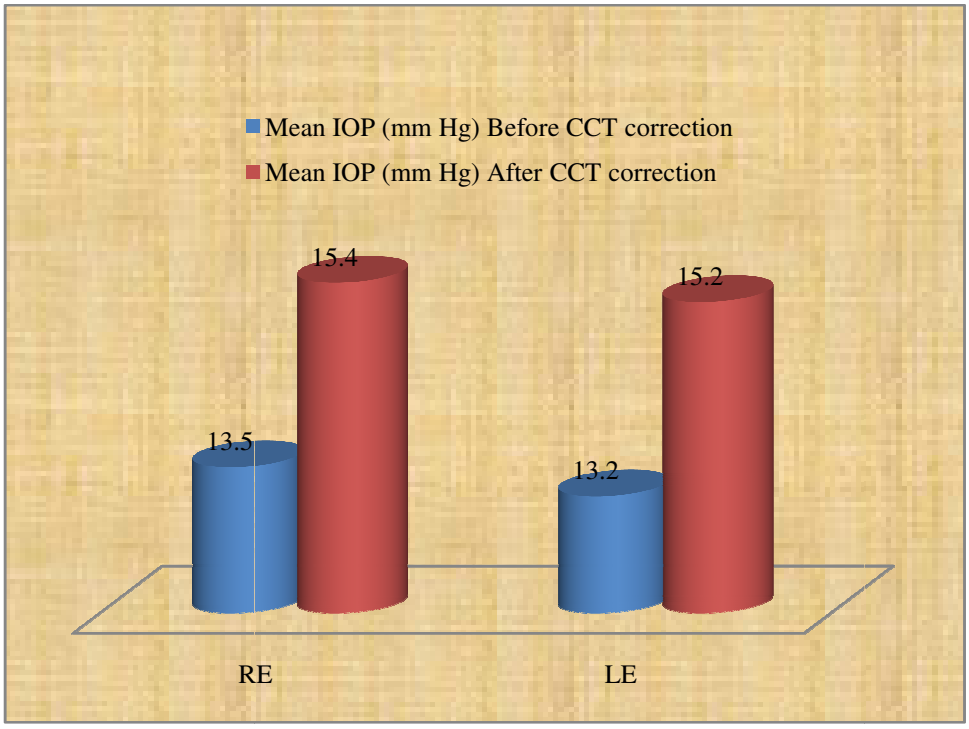


Table 18. Comparison of IOP before & after CCT correction in control group.

	Mean IOP (mm Hg)	
	Before CCT correction	**After CCT correction**
RE	13.5	15.4
LE	13.2	15.2

The above table shows that there is an increase in the IOP of about 1.9 mm Hg in RE and 2 mm Hg in LE after CCT correction in the control group. This increase in IOP was statistically significant. (P value=0.000)

Chart 18. IOP before & after CCT correction in control group.



Paired Samples Correlations

IOP before & after CCT Correction in Control group	N	Correlation	Sig.
	100	0.640	**0.000**

Paired Samples test

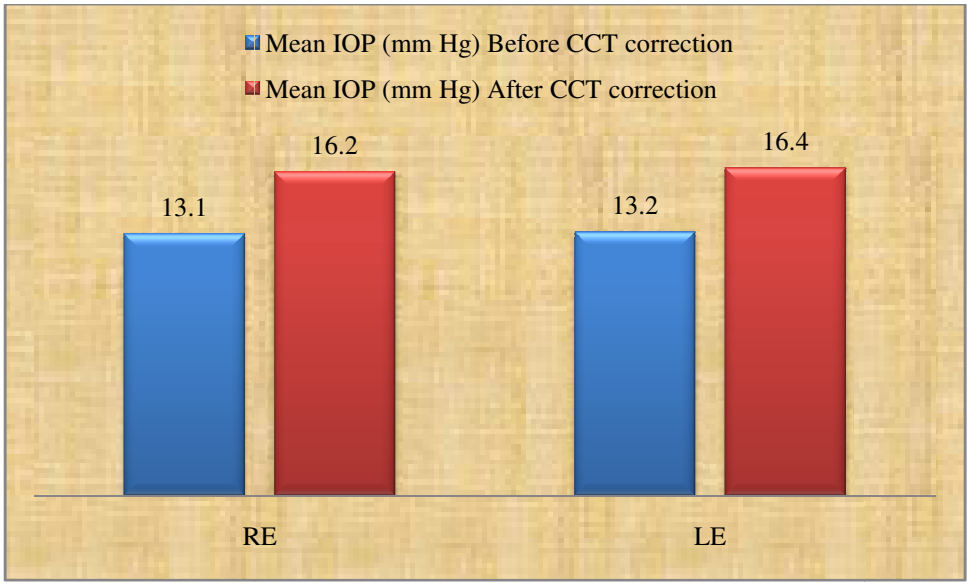
IOP	Paired differences					t	df	Sig. (2 tailed)
	Mean	Std deviation	Std error mean	95% Confidence Interval				
				Lower	Upper			
Before and after CCT Correction in Control group	-1.9505	2.3682	.23682	-2.4204	-1.4806	-8.236	99	**.000**

Table 19. Comparison of IOP before & after CCT correction in PEXF group.

	Mean IOP (mm Hg)	
	Before CCT correction	**After CCT correction**
RE	13.1	16.2
LE	13.2	16.4

The above table shows that there is an increase in the IOP of about 3.1mm Hg in RE and 3.2 mm Hg in LE after CCT correction in both eyes of the PEXF group. The increase in IOP was statistically significant. (P value=0.0)

Chart 19. IOP before and after CCT Correction in PEXF Group



Paired Samples Correlations

IOP before & after CCT Correction in Control group	N	Correlation	Sig.
	50	0.666	**0.000**

Paired Samples test

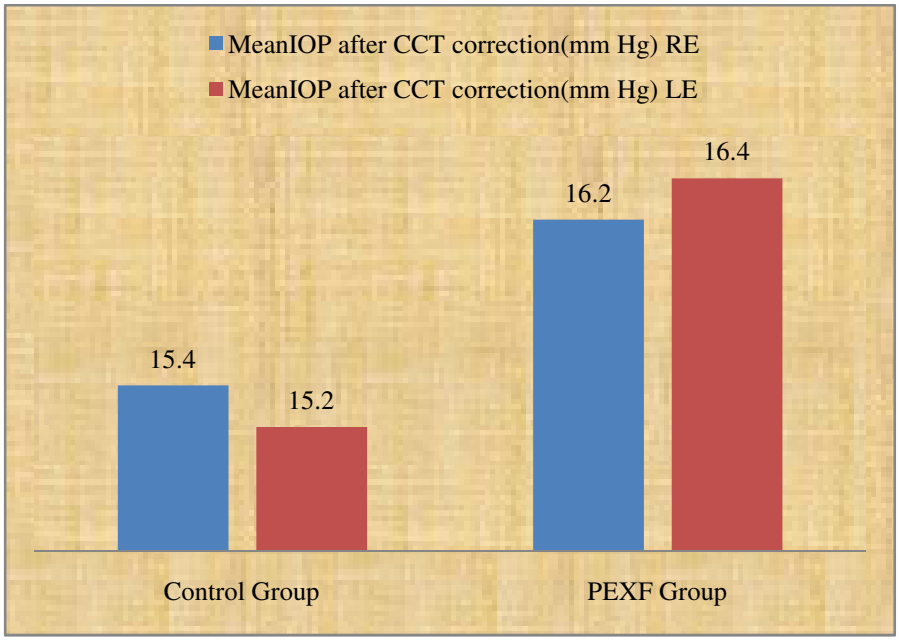
IOP	Paired differences							
	Mean	Std deviation	Std error mean	95% Confidence Interval		t	df	Sig. (2 tailed)
				Lower	Upper			
Before and after CCT Correction in Control group	-3.15000	2.34736	.33197	-3.76711	-2.43289	-9.338	49	**.000**

Table 20. Comparison of IOP after CCT correction between the control group and PEXFgroup.

	MeanIOP after CCT correction(mm Hg)	
	RE	**LE**
Control Group	15.4	15.2
PEXF Group	16.2	16.4

The above table shows that the IOP after CCT correction is higher in the PEXF group than the control group. The difference was statistically significant between the two groups.(P value=0.049)

Chart 20. Comparison of IOP between Control & PEXF group after CCT Correction



Paired Samples Correlations

Mean IOP after CCT Correction	N	Mean	Std. Deviation	Std. Error Mean
PEXF Group	50	16.2700	2.82391	.39936
Control Group	100	15.3105	2.77203	.27720

Paired Samples test

CCT	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	T	Df	Sig (2 tailed)	Mean diff	Std error of mean	95% Confidence Interval of the Difference	
								Lower	Upper
Eq.variance assumed	.247	.620	1.986	148	.049	.95950	.48312	.00479	1.91421
Eq.variances not assumed			1.974	96.503	.051	.95950	.48614	-.00541	1.92441

DISCUSSION

Pseudo exfoliation is the most common cause of secondary open angle glaucoma. The Blue Mountains eye study showed that the incidence of glaucoma in eyes with PEXF is 9 times higher (14.2%) than the eyes without PEXF (1.7%). [95]The eyes with PEXF have a higher risk, which is independent of other risk factors including IOP. [95]They are associated with a thinner CCT,[17] which leads to an underestimation of IOP and thereby a delayed diagnosis. Thinner CCT itself serves as another independent risk factor for development of glaucoma.[15] All these factors coupled together place the individuals with PEXF at a very high risk of advanced glaucomatous damage than primary open angle glaucoma.

As this study is hospital based, exact prevalence of pseudo exfoliation could not be estimated. However, the distribution of PEXF was found to be more among males both within the PEXF group and the overall population included in the study. This is in accordance with study by Krishnadas et al. [19] (The Aravind Comprehensive eye survey).

The distributionof PEXF was found to be apparently higher in the age group of 70-79 years. However, after matching for age between the study and control groups, the distribution of PEXF was greatest in those aged > 80 years

(60%) and least in those aged <60 years(25%). This is in accordance with various studies that have shown that prevalence of pseudo exfoliation increases with increasing age. Similar results were observed in the studies by Krishnadas et al.[19] (The Aravind Comprehensive eye survey) and Mitchell et al. [95] (The Blue Mountains eye study).

The CCT was evaluated using an ultrasonic pachymeter. A minimum of 3 measurements are required for an accurate measurement. [96]The reliability of measurements is fairly good in this study as five measurements were taken for each eye.

In the control group without PEXF, the mean CCT was 0.517 mm. There was no significant difference between both the eyes. Within the group, the CCT was slightly thinner in females when compared with males. This was similar to the study by Shimmyo et al. and various other studies. [8, 97] However, this difference was statistically insignificant. (P value = 0.388)

The mean CCT in PEXF group was 0.501 mm in RE and 0.500 mm in LE. There was no significant difference in CCT between both the eyes. In this group also, the CCT was slightly thinner in females than males. This difference was also statistically insignificant (P value RE= 0.492 LE= 0.339)

The analysis of CCT in both genders in the overall population included in the study also showed that the CCT was thinner in females than males. However, this too proved insignificant following statistical analysis (P value=0.436)

Different studies have shown that there is no difference in CCT between both genders [49] and few studies have shown that CCT is higher in females.[50]

Most of the studies have reported that CCT decreases with age. [8, 9, 10, 47, 48] But, in this study, a significant relationship was not established between age and CCT. The mean CCT was almost similar in all the groups. There was a decrease in CCT in those aged more than 80 years when compared with those aged less than 80 years. However, 60% of them had PEXF and hence the thinning was whether due to age or the presence of PEXF could not be ascertained. The difference was statistically insignificant too.(P value=0.352) Certain other studies have also shown that there is no significant relation between CCT and age.[97,98]

The comparison of CCT between the control group and the PEXF group showed that the CCT was thinner in the PEXF group than the control group without PEXF. This difference proved to be statistically significant too. (P value RE= 0.008 LE =0.003).

To support this, an overall comparison of the CCT was made between the 80 eyes with PEXF and the 220 eyes without PEXF (200 eyes of the control group and the 20 fellow eyes without PEXF in the unilateral group). This also showed a significant thinning of the central cornea in those 80 eyes with PEXF than the 220 eyes without PEXF. (P value=0.001)

This shows that the presence of pseudo exfoliation is strongly associated with a significant thinning of the cornea. This is attributed to the apoptosis of the keratocytes of the anterior corneal stroma. [30]Similar results were established by the studies by Hepsen et al , Mohammed Ali Zare et al.and various others.[17,79]

A still stronger evidence of the association of PEXF with a thinner CCT can be established if the CCT is compared between the eye with PEXF and the fellow eye without PEXF in the same individual. This may eliminate the age and gender related bias.

So far only very few studies have been reported analyzing the difference in CCT between both eyes with unilateral PEXF. One such study [83] showed that the CCT was thicker in the eye with PEXF than the fellow eye without PEXF. This was contradictory to all other studies which showed that PEXF is associated with thinner CCT. The limitation of this study was that it did not compare the CCT of either eyes with the normal population. Had there been a

comparison with normal population, the influence of PEXF on CCT could have been established still clearly.

In this study, the difference in CCT between the eye with PEXF and its fellow eye without PEXF was analyzed in the 20 patients with unilateral PEXF. The eyes with PEXF had a slightly thinner CCT (0.494 mm) than the eyes without PEXF (0.499mm). However, the difference was statistically insignificant (p value= 0.644).

Based on this alone, it cannot be concluded that the association of PEXF with thinner CCT in this study is only a coincidence. The fellow eyes of eyes with PEXF, though did not show evidence of PEXF by slit lamp examination, might have had occult deposition of PEXF material in the ocular structures which are too difficult to be detected by clinical examination.

This is supported by the discovery of the fact by Zheng et al. [30] who studied the ultra structural changes in eyes with unilateral PEXF by in vivo confocal microscopic examination and compared them with the fellow eyes without PEXF and also the control population without PEXF. They observed that the corneal endothelial cell density was significantly reduced in both the eyes with PEXF and their fellow eye without any clinical signs of PEXF. They also reported that there was evidence of deposition of hypereflective material suggestive of PEXF on the corneal endothelium, not only in the eyes with

PEXF but also in 51.9% of the fellow eyes without PEXF. The subbasal nerve plexus also showed changes in the fellow eyes similar to the eyes with PEXF. Therefore, they suggested that the fellow eyes could have been in a preclinical stage of PEXF. [30]

Few other studies have also shown that when one eye was affected by PEXF, the unaffected fellow eye had abnormal aqueous humour dynamics. Most of the unaffected fellow eyes demonstrated pigment related signs of PEXF. Almost all of the uninvolved fellow eyes demonstrated pseudo exfoliation material in conjunctival biopsy. [29, 99] Hence, they suggested that the term unilateral PEXF may be misleading. Most of the individuals with pseudo exfoliation have bilateral but asymmetric involvement which cannot be detected by clinical examination.

Based on the above studies, it can be explained that the 20 subjects with unilateral pseudo exfoliation in this study might have had asymmetric involvement with the fellow eyes without PEXF being at a preclinical stage and this could be the reason for the absence of any significant difference in the CCT between the two eyes.

A comparison of CCT was made between the 20 eyes without PEXF in the unilateral PEXF group and the 200 eyes without PEXF in control group.

The 20 fellow eyes of eyes with unilateral pseudo exfoliation though did not have any evidence of PEXF on slit lamp examination, had a significantly thinner CCT when compared with the 200 eyes of the control group. This difference, proved to be statistically significant too (P value=0.021). This too supports the fact that those 20 eyes might have been at a pre clinical stage of PEXF. However, more sophisticated techniques like in vivo con focal microscopic examination are required to support this fact.

The mean IOP before adjusting for CCT value was almost similar in both eyes of the control group. Following adjustment of the IOP values for the CCT values, there was an increase in the IOP of about 1.95 mm Hg in both the eyes. The increase in IOP was found to be statistically significant too. (P value= 0.000)

In the PEXF group, the average IOP before adjustment for CCT was 13.1mm Hg and 13.2 mm Hg in the right and left eyes respectively. The difference in IOP between both eyes was very minimal. Following adjustment of IOP for CCT, there was an increase of about 3.1 mm Hg in the IOP of both the eyes. The increase in IOP was statistically significant too. (P value=0.000)

Both the control and the PEXF groups had an almost similar IOP before CCT correction. There was a significant increase in the IOP following

adjustment for CCT in both the groups. This shows that the IOP has been underestimated by GAT in both the control group and the PEXF group. The underestimation in the IOP in the PEXF group can be explained by the presence of pseudo exfoliation and the associated significant corneal thinning which causes an underestimation.

However, there was an underestimation of IOP in the control group too which suggests that the CCT is thinner than the average in the control group too. The reason for thinner corneas in the study group, without any obvious local or systemic causes, is unclear. A possible explanation for this could be offered by the fact that the CCT differs in different population. Various studies have proven the same. [7, 43] Moreover, the definition of mean CCT has also been controversial. There is a wide variation within a given population. [44]While few studies show that the average CCT in Indian population is 0.520 mm, [45] there are few other studies which show that it is about 0.545 mm.[46] A prefixed mean CCT, therefore, cannot be applied for every population.

In this study, the pachymetry device used has been calibrated in such a way that the mean CCT is 0.545 mm. Any value below this, will underestimate the IOP and any value above this overestimates the IOP. The control group had a mean CCT of only 0.517 mm. This explains why there is an underestimation of IOP in them.

However, this mean CCT observed in the study population may not be applicable to the entire community. An exact estimation of the mean CCT can be estimated only through population based study. This study being hospital based cannot give an exact estimation of the average CCT.

The significant increase in IOP following adjustment of CCT even in the control groups observed in the study emphasizes the measurement of CCT in all the patients during glaucoma patients and adjusting the IOP measurements accordingly for an accurate measurement of the true IOP.

Although the mean CCT was slightly thinner in the control group, it was considered as the baseline CCT for the entire study population and the CCT in PEXF group was compared with it. The PEXF group demonstrated a still more thinning than the control group which was statistically significant too. This shows that there is a strong association of PEXF with thinner CCT.

Initially, the IOP before adjustment for CCT was similar in both the study and control groups and both the groups showed a significant increase in the IOP following adjustment for CCT. However this increase in IOP was dissimilar (1.9 mm Hg in the control group versus 3.1 mm Hg in the PEXF group). The CCT adjusted IOP was higher in the PEXF group than the control group and the difference was statistically significant too. (P value=0.049) The higher IOP in the PEXF group after CCT adjustment is explained by the fact

that the CCT is significantly thinner in them and therefore they had a more pronounced underestimation of the IOP than the control group.

Most of the studies have shown that the IOP is higher in eyes with PEXF than the eyes without PEXF. [100] A similar result was also obtained in this study. However, the difference between the 2 groups, although statistically significant, was not that higher as observed in other studies. The reason for this could be attributed to the measurement of IOP only once during the study. The diurnal variation of IOP was not taken into account. Studies by Altintas et al.[101] have shown that the diurnal variation in IOP is more pronounced in individuals with PEXF than those without PEXF. Measurement of diurnal variation of the IOP could have demonstrated a still higher IOP in the PEXF group than the control group.

This study has demonstrated that the CCT is thinner than average in both the study group and the control group and therefore emphasizes the measurement of CCT in all individuals for an accurate measurement of IOP. The PEXF group exhibited a still more significant thinning of the central cornea and a significantly higher risk of underestimation of IOP compared with the control group. The individuals with pseudo exfoliation are at greater risk of developing glaucoma than those without PEXF. A thinner CCT itself may act as an additional risk factor for development of glaucoma and along with this, there

is an underestimation of IOP resulting in a delay in diagnosis. All these factors lead to advanced disease at the time of presentation.

Measurement of CCT, therefore, is necessary in all cases of pseudo exfoliation for prediction of the risk of development and progression of glaucoma, for early diagnosis and to ensure adequacy of treatment.

CONCLUSION

The distribution of pseudo exfoliation was more common in males than females. The distribution of pseudo exfoliation was higher in older individuals than younger individuals. There was no significant relation between age and central corneal thickness. The mean CCT was slightly lower in females when compared with males in both individuals with pseudo exfoliation and without pseudo exfoliation. However, this difference proved to be statistically insignificant.

The CCT was significantly thinner in the eyes with pseudo exfoliation than the eyes without pseudo exfoliation. In individuals with bilateral pseudo exfoliation, there was no significant difference between both eyes. However, in the individuals with unilateral pseudo exfoliation, a slightly lower CCT was observed in the eye with pseudo exfoliation compared to the fellow eye without pseudo exfoliation. This difference, however, was statistically insignificant.

Moreover, both the eyes in individuals with unilateral pseudo exfoliation, irrespective of the presence or absence of pseudo exfoliation exhibited a statistically significant thinning when compared with the individuals without pseudo exfoliation. This suggests that the fellow eyes of eyes with PEXF might have been at a pre-clinical stage which can be demonstrated only by

ultrastructural studies like electron microscopy and in vivo confocal microscopy.

There was an underestimation of IOP by GAT in both the groups. However, the underestimation of IOP was more pronounced in the individuals with pseudo exfoliation.

Pseudo exfoliation itself is a major risk factor for the development of glaucoma. Being associated with thinner corneas which serve as another independent risk factor for the development and progression of glaucoma, the individuals with pseudo exfoliation are at still greater risk of developing glaucoma. The underestimation of the intra ocular pressure in these individuals further worsens the prognosis due to a delay in diagnosis and inadequate IOP control.

The measurement of CCT is therefore mandatory in the individuals with pseudo exfoliation syndrome to predict the risk of development of glaucoma, to facilitate early diagnosis and ensure adequacy of treatment.

SUMMARY

This study entitled 'Central corneal thickness in individuals with and without pseudo exfoliation syndrome' is a hospital based comparative study.

Individuals with pseudo exfoliation syndrome are at higher risk for developing glaucoma than those without pseudo exfoliation syndrome. When they are associated with thinner central corneal thickness, which is an independent risk factor for glaucoma development and progression, the risk of glaucomatous optic nerve damage increases many fold. They are likely to be diagnosed late because of an underestimation of IOP by applanation tonometry.

The aim of the study was to compare the CCT in individuals with pseudo exfoliation syndrome and those without pseudo exfoliation syndrome.

A total of 100 normal subjects without PXS and 50 subjects with PXS without any corneal pathology or glaucoma were included in the study. Their CCT and IOP were measured and compared. The influence of CCT on IOP measurements were analyzed in both the groups.

It was concluded that the CCT is thinner in individuals with PXS than those without PXS. In the patients with unilateral pseudo exfoliation syndrome, there was no significant difference between the eye with & without PXS. It was

presumed that the fellow eye without PEXF in individuals with unilateral PXS might have been at a preclinical stage. The IOP was underestimated in both the groups by applanation tonometry. However, the underestimation was more pronounced in individuals with PXS because of thinner CCT.

Thus, this study emphasizes the measurement of CCT in PXS to predict the risk of developing glaucoma, to facilitate early diagnosis and ensure appropriate management by an accurate measurement of IOP.

BIBLIOGRAPHY

1. Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol 1996;80:389-93.
2. Resnikoff et al. Bulletin of the WHO:In Focus 2004;844-51.
3. Sihota R, Tandon R. The Glaucomas. Parson's Diseases of the eye. 21st edition. New Delhi: Elsevier publishers;2011.p.280.
4. Wessels IF, Oh Y. Tonometer utilization, accuracy, and calibration under field conditions. Arch Ophthalmol 1990;108:1709–12.
5. Ehlers N, Bramsen T, Sperling S. Applanation tonometry and central corneal thickness. Acta Ophthalmol 1975; 53: 34-43.
6. Whitacre MM, Stein RA, Hassanein K. The effect of corneal thickness on applanation tonometry. Am J Ophthalmol 1993;115: 592-6.
7. La Rosa FA, Gross RL, Orengo-Nania S. Central corneal thickness of Caucasians and African Americans in glaucomatous and nonglaucomatous populations.Arch Ophthalmol 2001;119:23–7.
8. Europeon Glaucoma Prevention Study Group. Centralcorneal thickness in the Europeon Glaucoma Prevention Study. Ophthalmology 2007;114:454-9.
9. Brandt JD, Beiser JA, Kass MA, et al. Central corneal thickness in the Ocular Hypertension Treatment Study(OHTS). Ophthalmology 2001;108:1779-88.
10. Hahn S, Azen S, Ying-Lai M, et al. Central corneal thickness in Latinos. Invest Ophthalmol Vis Sci 2003;44:1508-12.

11. Kohlhaas M, Boehm AG, Spoerl, et al. Effect of central corneal thickness, corneal curvature, and axial length on applanation tonometry. Arch Ophthalmol 2006;124:471–6.
12. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. Surv Ophthalmol 2000;44:367–408.
13. Herndon LW, Choudhri SA, Cox T, et al. Central corneal thickness in normal, glaucomatous, and ocular hypertensive eyes. Arch Ophthalmol 1997;115:1137–41.
14. Copt RP, Thomas R, Mermoud A. Corneal thickness in ocular hypertension, primary open-angle glaucoma, and normal tension glaucoma. Arch Ophthalmol 1999;117:14–16.
15. Herndon LW, Weizer JS, Stinnett SS. Central corneal thickness as a risk factor for advanced glaucoma damage. Arch Ophthalmol 2004;122:17–21.
16. Alpeza-Dunato Z, Novak-Stroligo M, Kovacevic D, et al. Pseudoexfoliative Glaucoma. Coll Antropol 2011(35)2: 303–304.
17. Zare M A, Fakhraie G, Amoli F A, et al. Central Corneal Thickness, Corneal Endothelial Cell Density, and Lens Capsule Thickness in Normotensive Patients with and without Pseudoexfoliation Syndrome Iranian Journal of Ophthalmology 2012;24(2):47-51.
18. Lindberg JG. Clinical studies of depigmentation of the pupillary margin and transillumination of the iris in cases of senile cataract and also in normal eyes in the aged [Thesis]. Helsinki, Finland: Helsinki University; 1917.

19. Krishnadas R, Nirmalan PK, Ramakrishnan R, et al. Pseudoexfoliation in a rural population of southern India: the Aravind Comprehensive Eye Survey. Am J Ophthalmol 2003;135(6):830-7.
20. Aasved H. Mass screening for fibrillopathia epitheliocapsularis, so-called senile exfoliation or pseudoexfoliation of the anterior lens capsule. Acta Ophthalmol (Copenh) 1971;49(2):334-43.
21. Schlotzer-Schrehardt UM, Koca MR, Naumann GO, et al. Pseudoexfoliation syndrome. Ocular manifestation of a systemic disorder. Arch Ophthalmol 1992;110(12):1752-6.
22. Mitchell P, Wang JJ, Smith W. Association of pseudoexfoliation syndrome with increased vascular risk. Am J Ophthalmol 1997;124(5):685-7.
23. Ramprasad VL, George R, Soumittra N, Sharmila F, Vijaya L, Kumaramanickavel G. Association of non-synonymous single nucleotide polymorphisms in the LOXL1 gene with pseudoexfoliation syndrome in India. Mol Vis. 2008;14:318–22.
24. Thorleifsson G, Magnusson KP, Sulem P, et al. Common sequence variants in the LOXL1 gene confer susceptibility to exfoliation glaucoma. Science.2007;317:1397–1400.
25. Naumann G O H, Schlötzer-Schrehardt U, Kuchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist: intraocular and systemic manifestations. Ophthalmology 998;105:951–68.
26. Schlötzer-Schrehardt U, Naumann G O H. Ocular and systemic pseudoexfoliation syndrome. Am J Ophthalmol 2006;141:921–37.
27. Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. Surv Ophthalmol 2001;45:265–315.

28. Dickson DH, Ramsey MS. Symposium on pseudocapsular exfoliation and glaucoma. Fibrillopathia epitheliocapsularis: Review of the nature and origin of pseudoexfoliative deposits. Trans phthalmol Soc 1979;99(2):284-92.
29. Hammer T, Schlötzer-Schrehardt U,. Naumann GOH. Unilateral or Asymmetric Pseudoexfoliation Syndrome?An Ultrastructural Study. Arch Ophthalmol. 2001;119(7):1023-31.
30. Zheng X, Shiraishi A, Okuma S, et al. In Vivo Confocal Microscopic Evidence of Keratopathy in Patients with Pseudoexfoliation Syndrome. IOVS 2011;52(3):1755-61.
31. Detorakis ET, Koukoula S, Chrisohoou F, et al. Central corneal mechanical sensitivity in pseudoexfoliation syndrome. Cornea 2005;24:688–91.
32. Naumann G O H, Schlötzer - Schrehardt U. Keratopahty in pseudoexfoliation syndrome as a cause of corneal endothelial decompensation—a clinicopathologic study. Ophthalmology 2000;107:1111–24.
33. Abbott RL,Fine BS, Webster RB, et al. Specular microscopic and histologic observations in nonguttata corneal endothelial degeneration. Ophthalmology 1981;88:788–800.
34. Asano N, Schlötzer-Schrehardt U, Naumann GO, et al. A histopathologic study of iris changes in pseudoexfoliation syndrome. Ophthalmology, 1995;102(9):1279-90.
35. Orhan M, Karadeniz S, Erdener U, et al. Complications of extracapsular cataract extraction in patients with pseudoexfoliation syndrome. Eur J Implant Refractive Surg 1995; 7: 2–5.

36. Kozobolis VP, Christodoulakis EV, Naoumidi II, et al. Study of conjunctival goblet cell morphology and tear film stability in pseudoexfoliation syndrome. Graefes Arch Clin Exp Ophthalmol 2004;242:478–83.
37. Gross RJ, Tingey D, and Epstein DL: Increased prevalence of occludable angles and ACG in patients with pseudo exfoliation. Am J Ophthalmol 1994;117:333-6.
38. Lamba P A, Giridhar A. Pseudoexfoliation syndrome. Indian J Ophthalmol 1984;32:169-73.
39. Yalaz M, Othman I, Nas K, et al. The frequency of pseudoexfoliation syndrome in the Eastern Mediterranean area of Turkey. Acta Ophthalmologica 1992;70(2):209-13.
40. Samuel MJ, Randy A K, David OH, et al. The Risk of Glaucoma in Pseudoexfoliation Syndrome. Journal of Glaucoma 2007;16(1):117-21.
41. Majka C P, Challa P. Ophthalmic pearls: Glaucoma. Diagnosis and management of pseudo exfoliation glaucoma. Eye net magazine.
42. Pohjanpelto P: Long-term prognosis of visual field in glaucoma simplex and glaucoma capsulare Acta Ophthalmol 1985;63:418-23.
43. Karjalainen K, Tarkkanen A, Merenmies L: Exfoliation syndrome in enucleated haemorrhagic and absolute glaucoma Acta Ophthalmol 1987; 65:320-22.
44. Gunvant P, Baskaran M, Vijaya L, et al. Effect of corneal parameters on measurements using the pulsatile ocular blood flow tonograph and Goldmann applanation tonometer. Br J Ophthalmol 2004;88:518–22.
45. Racette L, Boden C, Kleinhandler SL, et al. Differences in visual function and optic nerve structure between healthy eyes of Blacks and Whites. Arch Ophthalmol 2005;123:1547–53.

46. Aghaian E, Choe JE, Lin S, et al.Central corneal thickness of Caucasians, Chinese, Hispanics, Filipinos, African Americans, and Japanese in a glaucoma clinic. Ophthalmology 2004 Dec;111(12):2211-9.
47. Kunert KS, Bhartiya P, Tandon R, et al. Central corneal thickness in Indian patients undergoing LASIK for myopia. J Refract Surg 2003;19:378-79.
48. Malik A, Relhan N, Singh M,et al. Central Corneal Thickness in Normal Indian Population. AIOC Proceedings 2010;326-8.
49. Foster PJ, Baasanhu J, Alsbirk PH, et al. Central corneal thickness and intraocular pressure in a Mongolian population. Ophthalmology 1998;15:969–73.
50. Alsbirk PH. Corneal Thickness.I. Age variation, sex, difference and oculometric correlations. Acta Ophthalmol Scand 1978;56:95–104.
51. Su DHW, Wong TY, Wong WL, et al. Diabetes,Hyperglycemia, and Central corneal thickness.Ophthalmology 2008;115:964-8.
52. Torres RJ, Jones E, Edmunds B, et al. Central Corneal Thickness in Northwestern American Indians/Alaskan Native and comparison with White and African – American Persons. Am J Ophthalmol 2008;146:747-51.
53. Ozcura F, Aydin S, Uzgoren N, et al. Effects of central corneal thickness, central corneal power, and axial length on intraocular pressure measurement assessed with Goldmann applanation tonometry. Jpn J Ophthalmol 2008*;*52*:*353–56.
54. Sanchez-Tocino H, Bringas-Calvo R, Iglesias-Cortinas D. Correlation between intraocular pressure, paquimetry and keratometry in a normal population. Arch Soc Esp Oftalmol 2007;82:267–72.

55. Chang SW, Tsai IL, Hu FR, et al. The cornea in young myopic adults. Br J Ophthalmol 2001;85:916–20.
56. Liu Z, Pflugfelder S. The effects of long-term contact lens wear on cornealthickness, curvature, and surface irregularity. Ophthalmology 2000;107: 105–11.
57. Joseph J K, Adamis A P. Corneal Pachymetry. In: Foster C S, editor. Smolin & Thoft's The Cornea, 4th edn. Philadelphila:Lippincott Williams & Wilkins;2005.p.161-5.
58. Mathew PT, David S, Thomas N. Endothelial cell loss and central corneal thickness in patients with and without diabetes after manual small incision cataract surgery. Cornea 2011;30(4):424-8.
59. Browning A C, Bhan A, Rotchford A P, et al. The effect of corneal thickness on intraocular pressure measurement in patients with corneal pathology. Br J Ophthalmol 2004;88:1395-99.
60. Sanchez-Thorin JC. The cornea in diabetes mellitus. Int Ophthalmol Clin 1998;38:19-36.
61. Monnier VM, Sell DR, Abdul-Karim FW, et al. Collagen browning and cross-linking are increased in chronic experimental hyperglycemia: Relevance to diabetes and aging. Diabetes 1988;37:867-72.
62. Su DH, Wong TY, Foster PJ, Central corneal thickness and its associations with ocular and systemic factors: the Singapore Malay Eye Study. Am J Ophthalmol 2009;147(4):709-16.
63. Varma R, Tielsch JM, Quigley HA, et al. Race, age, gender, and refractive error related differences in normal optic disc. Arch Ophthalmol 1994;112:1068–76.
64. Budde WM, Velten IM, Jonas JB. Optic disc size and iris color. Arch Ophthalmol 1998;116:545.

65. Patwardhan A A, Khan M, Mollan S P, et al. The importance of central corneal thickness measurements and decision making in general ophthalmology clinics: a masked observational study. BMC Ophthalmology 2008, 8:1.
66. Gordon M O, Betser J A, Brandt J D, et al. The Ocular Hypertension Treatment Study: Baseline factors that predict the onset of primary open angle glaucoma. Arch Ophthalmol 2002;120:714-20.
67. Jonas JB, Mardin CY, Schlotzer-Schrehardt U, et al. Morphometry of the human lamina cribrosa surface. Invest Ophthalmol Vis Sci 1991;32:401–5.
68. Tezel G, Trinkaus K, Wax MB. Alterations in the morphology of lamina cribrosa pores in glaucomatous eyes. Br J Ophthalmol 2004;88:251–6.
69. Bellezza AJ, Hart RT, Burgoyne CF. The optic nerve head as a biomechanical structure: initial finite element modeling. Invest Ophthalmol Vis Sci 2000;41:2991–3000.
70. Pakravan M, A Parsa A, Sanagou M, et al. Central corneal thickness and correlation to optic disc size: a potential link for susceptibility to glaucoma. Br J Ophthalmol 2007;91:26–28.
71. Skuta G L, Cantor L B, Weiss J S. Telescopes and optical instruments. In: Atebara N H, editor. Chapter 8; American Academy of Ophthalmology Canada: LEO Publishers; 2012-13.p.259-60.
72. Goldmann H, Schmidt T. Uber Applanations tonometric. Ophthalmologie 1957;134:221-42.
73. Hansen F K, Ehlers N. Elevated tonometer readings caused by thick corneas. Acta Ophthalmol Scand 1971;49: 775–8.

74. Christoph K, Shan L, Joyee C. Correlation between intraocular pressure, central corneal thickness, stage of glaucoma and demographic patient data. J Glaucoma. 2006;15: 91-7.
75. Memon M, Talpur K I, Rajpur A, et al. Correlation between Intra Ocular Pressure,Central Corneal Thickness and Glaucoma Stage in Patients with Primary Open Angle Glaucoma. Pak J Ophthalmol 2010; 26(4):197-200.
76. Tharwat H. Mokbel, Asaad A. Ghanem. Correlation of central corneal thickness and optic nerve head topography in patients with primary open angle glaucoma. Oman J Ophthalmol. 2010;3: 75-80.
77. Iyamu E, Ituah I. The relationship between central corneal thickness and intraocular pressure: a comparative study of normal and glaucoma subjects. Afr J Med Sci 2008; 37: 345-53.
78. Inoue K, Okugawa K, Oshika T, et al. Morphological Study of Corneal Endothelium and Corneal Thickness in Pseudoexfoliation Syndrome. Jpn J Ophthalmol 2003(47): 235–9.
79. Hepsen I F, Yagczi R, Keskin U. Morphological Study of Corneal Endothelium and Corneal Thickness in Pseudoexfoliation Syndrome. Can J Ophthalmol 2007;42(5):677-80.
80. Ozcura F, Aydin S, Dayanir V. Central corneal thickness and corneal curvature in pseudoexfoliation syndrome with and without glaucoma. J Glaucoma 2011 Sep;20(7):410-3.
81. Gorezis S, Christos G, Stefaniotou M,et al. Comparative Results of Central Corneal Thickness Measurements in Primary Open-Angle Glaucoma, Pseudoexfoliation Glaucoma, and Ocular Hypertension. Ophthalmic Surg Lasers Imaging 2008;39(1): 17-21.

82. Sorkhabi R, Rahbani M B, Ahoor M H, et al. Retinal Nerve Fiber Layer and Central Corneal Thickness in Patients with Exfoliation Syndrome.Iranian Journal of Ophthalmology 2012;24(2):40-46.
83. Puska P, Vasara K, Harju M, et al. Corneal thickness and corneal endothelium in normotensive subjects with unilateral exfoliation syndrome. Graefes Arch Clin Exp Ophthalmol. 2000 Aug;238(8):659-63.
84. Popovic – Suic S, Kuzman T, Kordic R, et al.Is Central corneal thickness a risk factor for pseudo exfoliation glaucoma? Acta Clin Croat 2007;46(1):95-7.
85. Ventura A C, Bohnke M, Mojon D S. Central corneal thickness measurements in patients with normal tension glaucoma, primary open angle glaucoma, pseudo exfoliation glaucoma or ocular hypertension. Br J Ophthalmol 2001;85:792-5.
86. Okumus S, Tatar M G, Gungor K,et al. Comparison of central corneal thickness, corneal curvature and axial length values in pseudoexfoliation cases with or without cataract. Gaziantep Med J. 2011; 17(3): 137-140
87. Civcic N M. Eur J Ophthalmol 2011; 00(00).
88. Kitsos G, Gartzios C, Asproudis I, et al. Central corneal thickness in subjects with glaucoma and in normal individuals(with or without pseudoexfoliation syndrome). Clinical Ophthalmology 2009:3 537–42.
89. Sen E, Nalcacioglu P, Yazici A, et al. Comparison of the effects of latanoprost and bimatoprost on central corneal thickness. J Glaucoma 2008;17(5):398–402.
90. Stefaniotou M, Kalogeropoulos C, Razis N, et al. The Cornea in Exfoliation syndrome. Doc Ophthalmol 1992; 80(4):329-33.

91. Arnarsson A, Damji KF, Sverrisson T, et al. Pseudoexfoliation in the Reykjavik Eye Study: prevalence and related ophthalmological variables. Acta Ophthalmol Scand. 2007;85(8):822–7.
92. Yeshigeta Gelaw. The impact of central corneal thickness on intraocular pressure among Ethiopian glaucoma patients: a cross-sectional study. BMC Ophthalmol 2012;12: 58.
93. Yagci R, Eksioglu U, Midillioglu I, et al. Central corneal thickness in primary open angle glaucoma, pseudoexfoliative glaucoma, ocular hypertension, and normal population. Eur J Ophthalmol 2005;15(3):324–8.
94. Bechmann M, Thiel MG, Roesen B, et al. Central corneal thickness determined with optical coherence tomography in various types of glaucoma. Br J Opthalmol. 2000;84:688–691.
95. Mitchell P, Wang JJ, Hourihan F. The relationship between glaucoma and pseudoexfoliation: The Blue Mountains Eye Study. Arch Ophthalmol 1999;117(10):1319-24.
96. Realini T, Lovelace K. Measuring central corneal thickness with ultrasound pachymetry 2003 Jun;80(6):437-9.
97. Shimmyo M, Ross AJ, Moy A, et al. Intraocular pressure, Goldmann applanation tonometer, Corneal thickness, and Corneal curvature in Caucasions, Asians, Hispanics, and African Americans. Am J Ophthalmol 2003;136:603-13.
98. Wolfs RC, Klaver CC, Vingerling JR, et al. Distribution of central corneal thickness and its association with intraocular pressure: The Rotterdam Study. Am J Ophthalmol 1997;123:767–72.
99. Prince AM, Streeten BW, Ritch R, et al: Preclinical diagnosis of pseudoexfoliation syndrome Arch Ophthalmol 1987;105:1076-82.

100. Davanger, M., Ringvold, A. and Blika, S. Pseudo-exfoliation, IOP and glaucoma. Acta Ophthalmologica 1991;69: 569–73.
101. Altintas O, Yuksel N, Karabas V L. Diurnal intraocular pressure variation in pseudoexfoliation syndrome. Eur J Ophthalmol 2004;14(6):495 – 500.

PROFORMA

Name:

Age:

Sex: **Male/ Female.**

OP/IP No.:

Occupation:

Complaints:

History:

- History of ocular trauma: Yes/ No
- History of intra ocular surgeries: Yes/No
- History of contact lens wear: Yes/No
- History of glaucoma: Yes/No
- History of uveitis: Yes/No
- History of corneal disease: Yes/No
- History of any other ocular diseases: Yes/No
- History of medications for any ocular disease: Yes/ No
- History of diabetes mellitus: Yes/No

Ocular examination:

Visual acuity	**OD**	**OS**
Anterior segment examination with a slit lamp		
	OD	**OS**
Lids		
Conjunctiva		
Cornea		
Anterior chamber		
Iris		
Pupil		
Presence of pseudo exfoliation		
Lens		
Extra ocular movements		
Visual field examination		
IOP (by GAT)		
CCT (by ultrasound pachymetry)		
IOP after adjustment for CCT		
Gonioscopy		
Slit lamp examination with a dilated pupil		
	OD	**OS**
Pseudo exfoliation on anterior lens capsule		
Refraction		
Fundus examination		
DIAGNOSIS:		
Random blood sugar:		
BP:		
Urine sugar:		

CONSENT FORM

I hereby consent to participate in this study entitled 'CENTRAL CORNEAL THICKNESS IN INDIVIDUALS WITH AND WITHOUT PSEUDOEXFOLIATION SYNDROME'. I have been explained in detail about the nature of the study by the doctor knowing which I Mr. / Ms. …….. wholeheartedly volunteer to participate in this study.

Signature of the Volunteer

Signature of the witness

Date:

KEY TO MASTER CHART

M-Male

F- Female

RE Right Eye

LE Left Eye

SIMC- Senile Immature Cataract

SMC- Senile Mature Cataract

V/A- Visual acuity

HM- Hand Movements

CFCF- Counting Fingers Close to Face.

PEXF- Pseudo exfoliation

+ Presence of PEXF

- Absence of PEXF

IOP- Intra ocular Pressure

CCT-Central Corneal Thickness

BP- Blood Pressure

RBS- Random Blood Sugar

U/S- Urine sugar

SL NO	OP/IP No.	AGE	SEX	DIAGNOSIS		PEXF		VISUAL ACUITY		IOP		MEAN CCT		IOP AFTER CCT CORRECTION		RBS	BP	U/S
				RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE			
1	17538	63	M	SIMC	SIMC	_	_	6/18	6/12	19	19	0.565	0.573	17.6	17	102	120/80	_
2	10766	60	M	SIMC	SIMC	_	_	5/60	6/60	16	16	0.534	0.534	16.7	16.7	98	110/80	_
3	12346	67	M	SIMC	SIMC	_	_	5/60	6/18	18	18	0.578	0.582	15.7	15.4	84	120/90	_
4	4588	70	F	SIMC	SIMC	_	_	6/36	6/36	10	10	0.534	0.534	10.7	10.7	78	110/70	_
5	67108	55	F	SIMC	SIMC	_	_	2/60	6/36	8	8	0.492	0.49	11.7	11.9	96	110/70	_
6	67049	85	M	SIMC	SIMC	_	_	6/24	2/60	14	14	0.453	0.464	20.5	19.7	121	120/70	_
7	67119	50	M	SIMC	SIMC	_	_	6/18	1/60	12	12	0.551	0.55	11.6	11.6	129	110/70	_
8	67106	50	M	SIMC	SIMC	_	_	6/36	2/60	16	16	0.535	0.535	16.7	16.7	118	120/80	_
9	67260	74	M	SIMC	SIMC	_	_	6/18	6/24	14	14	0.531	0.525	15	15.4	85	120/80	_
10	67519	50	F	SIMC	SIMC	_	_	6/18	6/18	14	14	0.506	0.51	16.7	16.4	124	150/80	_
11	67579	60	M	SIMC	SIMC	_	_	6/36	6/36	15	16	0.501	0.501	18.1	19.1	97	160/100	_
12	67491	53	M	SIMC	SIMC	_	_	3/60	3/60	16	19	0.541	0.56	16.3	18	113	160/100	_
13	67578	55	M	SIMC	SIMC	_	_	4/60	4/60	10	11	0.475	0.475	14.9	15.9	92	140/80	_
14	67520	65	F	SIMC	SMC	_	_	6/18	HM	12	12	0.502	0.502	15	15	139	130/80	_
15	67580	61	M	SIMC	SIMC	_	_	4/60	5/60	12	12	0.566	0.561	10.6	10.9	139	120/80	_
16	67810	65	M	SIMC	SIMC	_	_	4/60	6/60	14	12	0.487	0.489	18.1	15.9	76	170/100	_
17	67811	74	F	SIMC	SIMC	_	_	4/60	3/60	10	10	0.49	0.502	13.9	13	83	130/60	_
18	67809	63	M	SIMC	SIMC	_	_	1/60	4/60	13	13	0.508	0.512	15.6	15.3	79	110/70	_
19	68208	60	F	SIMC	SIMC	_	_	4/60	1/60	16	16	0.502	0.486	19	20.2	92	110/70	_
20	68027	50	F	SIMC	SIMC	_	_	6/60	6/60	17	17	0.564	0.549	15.7	16.7	85	130/90	_
21	68486	65	M	SIMC	SIMC	_	_	6/24	2/60	10	10	0.545	0.534	10	10.7	112	170/110	_
22	74835	65	F	SIMC	SIMC	_	_	6/24	6/36	14	12	0.533	0.53	14.8	13	83	120/80	_
23	17564	65	M	SIMC	SIMC	_	_	6/60	6/24	9	9	0.469	0.474	14.3	13.9	83	120/80	_
24	68343	55	F	SMC	SIMC	_	_	HM	1/60	14	12	0.569	0.565	12.3	10.6	85	120/80	_
25	17630	68	F	SMC	SMC	_	_	1/60	HM	14	14	0.561	0.552	12.9	13.5	120	140/80	_
26	68488	60	F	SIMC	SIMC	_	_	6/24	1/60	14	10	0.534	0.534	14.7	10.7	136	200/100	_
27	17334	50	M	SIMC	SIMC	_	_	2/60	3/60	13	12	0.436	0.453	20.6	18.5	117	150/100	_
28	68029	70	F	SIMC	SIMC	_	_	6/18	6/24	14	16	0.562	0.551	12.8	15.6	119	150/90	_
29	17413	72	F	SIMC	SIMC	_	_	3/60	6/36	12	14	0.497	0.494	15.4	17.6	109	140/90	_
30	68030	90	M	SIMC	SIMC	_	_	6/60	5/60	14	12	0.469	0.469	19.3	17.3	93	170/90	_
31	68485	60	F	SIMC	SIMC	_	_	2/60	6/36	18	17	0.502	0.504	21	19.8	138	150/80	_
32	17352	73	M	SIMC	SIMC	_	_	6/36	6/24	10	10	0.528	0.524	11.2	11.5	128	120/80	_
33	17563	60	M	SIMC	SMC	_	_	6/36	HM	15	14	0.556	0.551	14.3	13.6	89	110/70	_
34	13084	50	M	SIMC	SIMC	_	_	6/60	6/60	12	12	0.508	0.501	14.6	15.1	92	110/70	_
35	17706	75	F	SIMC	SIMC	_	_	5/60	6/60	16	16	0.549	0.552	15.7	15.5	122	130/80	_
36	68772	65	F	SIMC	SIMC	_	_	6/24	6/24	18	15	0.551	0.552	17.6	14.5	138	120/80	_
37	68778	50	F	SIMC	SIMC	_	_	4/60	6/36	14	13	0.502	0.502	17	16	101	100/70	_
38	68770	65	F	SIMC	SIMC	_	_	6/24	6/36	14	16	0.551	0.551	13.6	15.6	89	140/100	_
39	68769	65	F	SIMC	SIMC	_	_	6/24	6/36	13	12	0.521	0.519	14.7	13.8	123	130/90	_
40	68768	62	F	SIMC	SIMC	_	_	6/36	6/60	14	13	0.529	0.519	15.1	14.8	92	140/100	_
41	68775	62	F	SIMC	SIMC	_	_	6/36	3/60	10	11	0.485	0.482	14.2	15.4	139	150/100	_
42	68780	65	F	SIMC	SIMC	_	_	6/24	6/36	14	10	0.472	0.479	19.1	14.6	127	130/80	_

43	68774	62	F	SMC	SIMC	_	_	CFCF	3/60	14	14	0.543	0.545	14.1	14	130	130/90	_
44	68771	65	F	SIMC	SIMC	_	_	2/60	4/60	12	10	0.534	0.534	12.7	10.7	111	140/100	_
45	68766	58	F	SIMC	SIMC	_	_	6/36	1/60	10	10	0.471	0.47	15.2	15.2	79	110/70	_
46	68924	78	M	SIMC	SIMC	_	_	6/36	4/60	16	16	0.516	0.489	18	19.9	90	130/80	_
47	68904	53	M	SIMC	SIMC	_	_	6/24	6/18	15	16	0.537	0.512	15.5	18.3	134	130/80	_
48	68959	78	M	SIMC	SIMC	_	_	5/60	1/60	10	8	0.508	0.502	12.6	11	96	100/70	_
49	69028	70	F	SMC	SIMC	_	_	HM	1/60	14	12	0.513	0.502	16.2	15	110	110/70	_
50	69279	60	F	SIMC	SIMC	_	_	1/60	1/60	16	14	0.554	0.555	15.4	13.3	125	90/60	_
51	69280	67	M	SIMC	SMC	_	_	6/18	HM	10	8	0.502	0.503	13	10.9	123	160/90	_
52	69281	66	F	SIMC	SIMC	_	_	6/60	5/60	14	14	0.485	0.484	18.2	18.2	95	130/80	_
53	69232	50	F	SIMC	SIMC	_	_	1/60	2/60	10	10	0.55	0.548	9.6	9.8	92	100/80	_
54	17697	50	F	SIMC	SMC	_	_	6/60	HM	8	8	0.5	0.502	11.1	11	123	100/70	_
55	70081	75	F	SIMC	SIMC	_	_	6/60	2/60	18	18	0.566	0.569	16.6	16.3	85	160/90	_
56	17590	55	F	SIMC	SIMC	_	_	1/60	2/60	10	11	0.487	0.485	14.1	15.2	132	140/80	_
57	70080	60	M	SIMC	SIMC	_	_	6/36	6/60	12	10	0.469	0.483	17.3	14.3	120	130/80	_
58	70042	60	F	SIMC	SIMC	_	_	6/36	2/60	12	12	0.567	0.58	10.4	9.6	136	140/70	_
59	70121	67	M	SIMC	SIMC	_	_	2/60	1/60	20	23	0.549	0.585	19.7	20.2	130	120/70	_
60	70064	57	M	SIMC	SIMC	_	_	6/36	6/36	13	10	0.506	0.502	15.7	13	60	110/80	_
61	70353	53	M	SIMC	SIMC	_	_	6/18	1/60	13	13	0.485	0.491	17.2	16.8	80	140/80	_
62	70355	65	F	SIMC	SIMC	_	_	5/60	6/60	16	15	0.501	0.504	19.1	17.8	65	140/100	_
63	70354	55	F	SIMC	SIMC	_	_	6/18	6/18	18	17	0.508	0.503	20.6	20.9	72	160/90	_
64	70364	60	F	SIMC	SIMC	_	_	5/60	6/36	12	12	0.516	0.522	14	13.6	90	110/70	_
65	70365	75	M	SIMC	SIMC	_	_	6/60	4/60	11	12	0.532	0.534	11.9	12.7	89	140/90	_
66	18444	58	F	SMC	SIMC	_	_	CFCF	6/24	12	14	0.525	0.518	13.4	15.9	103	130/80	_
67	70360	55	F	SIMC	SIMC	_	_	6/24	6/36	14	14	0.534	0.534	14.7	14.7	98	120/80	_
68	72005	64	F	SIMC	SIMC	_	_	3/60	6/60	16	16	0.548	0.545	15.8	16	106	110/70	_
69	70347	70	F	SIMC	SIMC	_	_	6/60	6/60	13	14	0.485	0.485	17.2	18.2	72	170/100	_
70	70351	55	F	SIMC	SIMC	_	_	6/60	1/60	13	14	0.469	0.469	18.3	19.3	75	130/80	_
71	70354	70	M	SIMC	SIMC	_	_	2/60	6/36	11	11	0.534	0.528	11.7	12.2	80	130/90	_
72	70726	50	M	SIMC	SIMC	_	_	6/36	6/36	14	14	0.551	0.548	13.6	13.8	102	130/80	_
73	70747	70	F	SIMC	SIMC	_	_	1/60	4/60	14	13	0.484	0.485	18.3	17.2	81	160/100	_
74	70827	60	F	SIMC	SIMC	_	_	6/36	5/60	12	12	0.462	0.453	17.8	18.5	108	110/80	_
75	70177	50	M	SIMC	SIMC	_	_	2/60	4/60	16	16	0.502	0.504	19	18.8	140	170/110	_
76	70933	65	F	SIMC	SIMC	_	_	6/60	1/60	20	20	0.537	0.543	20.5	20.1	98	180/100	_
77	71024	59	M	SIMC	SIMC	_	_	6/36	6/24	20	21	0.578	0.584	17.7	18.3	128	120/80	_
78	71076	70	F	SIMC	SMC	_	_	6/60	CFCF	14	14	0.51	0.483	16.5	18.3	103	200/100	_
79	71273	65	F	SIMC	SIMC	_	_	4/60	5/60	12	12	0.492	0.485	15.7	16.2	83	120/80	_
80	71272	65	F	SIMC	SIMC	_	_	6/60	5/60	15	16	0.491	0.497	18.8	19.4	86	110/80	_
81	71276	70	F	SIMC	SIMC	_	_	5/60	6/36	10	10	0.483	0.485	14.3	14.2	78	110/80	_
82	17955	50	F	SIMC	SIMC	_	_	1/60	1/60	14	12	0.585	0.585	11.2	9.2	76	110/80	_
83	17988	74	M	SIMC	SIMC	_	_	6/24	6/36	14	10	0.522	0.523	15.6	11.5	112	140/90	_
84	17978	57	M	SIMC	SIMC	_	_	1/60	5/60	17	17	0.538	0.536	17.5	17.6	120	130/80	_
85	17846	76	M	SIMC	SIMC	_	_	2/60	6/36	14	13	0.505	0.508	16.8	15.6	135	140/80	_
86	17875	55	F	SIMC	SIMC	_	_	6/18	6/18	13	12	0.469	0.469	18.3	17.3	129	130/80	_
87	31575	60	F	SMC	SIMC	_	_	HM	6/60	10	10	0.521	0.518	11.7	11.9	97	130/80	_

88	72009	68	M	SIMC	SIMC	_	_	6/24	6/24	13	13	0.518	0.524	14.9	14.5	93	130/80	_
89	72007	65	M	SIMC	SIMC	_	_	3/60	3/60	12	12	0.533	0.529	12.8	13.1	66	170/90	_
90	71994	60	M	SIMC	SIMC	_	_	3/60	6/36	10	11	0.503	0.512	13	13.3	50	140/90	_
91	72012	58	M	SIMC	SIMC	_	_	4/60	6/60	13	13	0.582	0.584	10.4	10.3	87	110/80	_
92	72008	52	F	SIMC	SIMC	_	_	6/24	6/60	16	16	0.534	0.526	16.7	17.3	95	120/80	_
93	71999	70	F	SIMC	SIMC	_	_	2/60	5/60	12	11	0.536	0.538	12.6	11.5	108	140/80	_
94	72003	65	F	SIMC	SIMC	_	_	3/60	6/36	8	10	0.436	0.468	15.6	15.4	103	200/100	_
95	72000	60	F	SIMC	SIMC	_	_	6/60	4/60	10	10	0.485	0.485	14.2	14.2	93	110/80	_
96	71998	68	F	SIMC	SIMC	_	_	6/36	6/60	13	13	0.436	0.436	20.6	20.6	82	160/90	_
97	72004	60	F	SIMC	SIMC	_	_	6/24	5/60	18	18	0.518	0.518	19.9	19.9	114	150/90	_
98	71995	60	F	SIMC	SIMC	_	_	2/60	4/60	10	8	0.469	0.485	15.3	12.2	77	140/90	_
99	71990	60	F	SIMC	SMC	_	_	4/60	HM	16	16	0.56	0.55	14.9	15.6	84	160/90	_
100	72006	60	F	SIMC	SIMC	_	_	3/60	2/60	14	15	0.534	0.534	14.7	15.7	92	100/80	_
101	12261	62	M	SIMC	SIMC	+	+	3/60	4/60	16	17	0.489	0.493	19.9	20.6	115	120/70	_
102	4305	75	M	SMC	SIMC	+	+	HM	3/60	14	16	0.526	0.523	15.2	17.6	70	130/80	_
103	11311	66	F	SIMC	SIMC	+	+	4/60	5/60	14	14	0.453	0.453	20.5	20.5	101	110/70	_
104	10769	70	M	SMC	SMC	+	_	CFCF	HM	13	13	0.453	0.453	19.5	19.5	106	130/80	_
105	1757	60	M	SIMC	SIMC	+	+	6/18	6/24	12	11	0.493	0.497	15.7	14.4	98	120/80	_
106	6681	60	F	SIMC	SIMC	+	+	6/24	3/60	12	12	0.519	0.518	13.2	13.4	105	110/70	_
107	6677	65	F	SIMC	SIMC	+	+	6/36	6/60	11	12	0.521	0.518	12.7	13.9	121	120/80	_
108	6526	61	M	SIMC	SIMC	+	+	3/60	6/24	10	12	0.498	0.5	13.3	15.1	123	130/80	_
109	10698	53	M	SIMC	SIMC	+	_	6/60	HM	7	10	0.485	0.496	11.2	13.5	0.3	150/90	_
110	4285	65	F	SIMC	SIMC	+	+	4/60	2/60	10	10	0.485	0.485	14.2	14.2	88	120/80	_
111	4974	70	M	SIMC	SIMC	+	+	6/24	5/60	12	12	0.502	0.516	15	14.1	98	160/100	_
112	5044	56	M	SIMC	SMC	_	+	6/36	1/60	14	14	0.492	0.485	17.7	18.2	126	100/80	_
113	3051	71	M	SIMC	SIMC	+	+	6/36	2/60	22	20	0.629	0.61	16.1	15.5	101	110/70	_
114	3075	67	M	SIMC	SIMC	+	_	6/36	4/60	14	16	0.512	0.518	16.3	17.9	84	120/80	_
115	22236	70	F	SIMC	SIMC	+	+	3/60	6/60	14	14	0.497	0.481	17.4	18.4	76	110/80	_
116	22175	70	M	SMC	SIMC	_	+	HM	6/60	13	12	0.534	0.518	13.7	13.9	132	120/80	_
117	41645	65	M	SIMC	SIMC	+	+	5/60	1/60	13	14	0.485	0.51	17.2	16.5	112	110/80	_
118	67365	50	M	SIMC	SIMC	+	_	2/60	2/60	10	10	0.502	0.486	13	14.2	106	110/70	_
119	67239	50	M	SIMC	SIMC	_	+	3/60	6/60	10	10	0.468	0.468	15.4	15.4	106	150/60	_
120	68026	68	F	SIMC	SIMC	_	+	6/18	2/60	18	18	0.554	0.534	17.4	18.7	112	150/90	_
121	68489	66	M	SIMC	SIMC	+	_	4/60	6/18	9	10	0.534	0.535	9.7	10.7	140	120/80	_
122	68767	75	M	SIMC	SIMC	+	+	3/60	5/60	18	18	0.502	0.504	21	20.8	124	130/90	_
123	68773	65	F	SIMC	SIMC	+	+	6/24	6/36	16	16	0.476	0.472	20.8	20.1	131	150/90	_
124	68779	62	M	SIMC	SIMC	_	+	6/60	3/60	13	14	0.58	0.571	10.6	12.2	133	120/80	_
125	69029	70	F	SIMC	SIMC	+	+	6/24	6/36	14	15	0.535	0.518	14.7	16.9	129	120/80	_
126	17812	67	F	SIMC	SIMC	+	+	6/24	6/18	18	18	0.542	0.548	18.2	17.8	102	110/70	_
127	70351	78	F	SIMC	SIMC	+	+	6/60	1/60	12	11	0.534	0.534	12.7	11.7	84	130/90	_
128	70347	70	F	SIMC	SIMC	+	+	5/60	2/60	10	10	0.523	0.518	11.5	11.9	78	120/80	_
129	70348	80	F	SIMC	SIMC	+	_	2/60	2/60	10	10	0.485	0.485	14.2	14.2	75	120/90	_
130	17438	65	F	SIMC	SIMC	_	+	6/60	4/60	10	10	0.453	0.469	16.5	15.3	98	100/70	_
131	70826	75	F	SMC	SIMC	+	+	HM	1/60	17	17	0.534	0.534	17.7	17.7	134	140/80	_
132	71079	75	F	SMC	SIMC	+	+	CFCF	3/60	18	18	0.524	0.534	19.5	18.7	74	180/100	_

133	70576	90	M	SIMC	SIMC	+	+	1/60	3/60	14	14	0.485	0.485	18.2	18.2	138	130/70	_
134	71075	65	F	SIMC	SIMC	+	+	6/36	6/36	10	10	0.436	0.436	17.6	17.6	94	130/80	_
135	71078	70	F	SIMC	SIMC	+	+	4/60	3/60	15	14	0.535	0.534	15.7	14.7	89	110/80	_
136	72011	50	M	SIMC	SIMC	_	+	3/60	4/60	14	14	0.502	0.502	17	17	64	110/80	_
137	72007	55	M	SIMC	SIMC	_	+	6/36	1/60	17	17	0.512	0.501	19.3	20.1	87	140/90	_
138	72027	50	M	SIMC	SIMC	+	+	2/60	5/60	13	14	0.502	0.502	16	17	72	110/70	_
139	71993	85	M	SMC	SMC	+	+	HM	1/60	9	9	0.483	0.488	13.3	13	59	150/90	_
140	72235	72	F	SIMC	SIMC	_	+	6/60	3/60	10	10	0.502	0.483	13	14.3	119	200/110	_
141	72108	65	M	SIMC	SIMC	_	+	4/60	5/60	10	7	0.498	0.485	13.3	11.2	107	130/80	_
142	72106	55	M	SIMC	SIMC	+	+	3/60	6/36	14	14	0.507	0.507	16.7	16.7	82	120/80	_
143	18233	55	F	SIMC	SIMC	+	_	6/60	6/60	15	16	0.469	0.485	20.3	20.2	88	120/80	_
144	72709	70	F	SIMC	SIMC	+	+	6/60	4/60	14	14	0.453	0.453	20.5	20.5	86	110/70	_
145	72713	70	F	SIMC	SIMC	_	+	3/60	2/60	14	14	0.469	0.469	19.3	19.3	67	100/60	_
146	72715	50	M	SIMC	SIMC	+	+	6/36	6/36	11	10	0.502	0.504	14	12.9	102	100/60	_
147	72721	65	F	SIMC	SIMC	+	_	6/60	4/60	12	11	0.469	0.453	17.3	17.5	99	120/80	_
148	72714	70	M	SIMC	SIMC	+	_	1/60	2/60	16	16	0.485	0.496	20.2	19.5	122	120/80	_
149	73346	72	M	SIMC	SIMC	+	+	6/60	4/60	12	12	0.453	0.453	18.5	18.5	96	110/80	_
150	73701	75	F	SMC	SIMC	+	+	HM	3/60	12	11	0.469	0.472	17.3	16.1	78	100/60	_